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SYMPOSIUM ON ANTHRAX IN MAN

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PHILADELPHIA, PENNSYLVANIA OCTOBER 8, 1954

DEPARTMENT OF HEALTH, COMMONWEALTH OF PENNSYLVANIA
DEPARTMENT OF PUBLIC HEALTH, CITY OF PHILADELPHIA
SCHOOL OF MEDICINE, UNIVERSITY OF PENNSYLVANIA

PROCEEDINGS OF THE

SYMPOSIUM

ON

ANTHRAX IN MAN

Presented Under the Joint Sponsorship of the
DEPARTMENT OF HEALTH, COMMONWEALTH OF PENNSYLVANIA
DEPARTMENT OF PUBLIC HEALTH, CITY OF PHILADELPHIA
SCHOOL OF MEDICINE, UNIVERSITY OF PENNSYLVANIA.

October 8, 1954

HOSPITAL of the UNIVERSITY OF PENNSYLVANIA
Philadelphia, Pa.

MORNING SESSION

Presiding: Harry E. Morton, Sc. D., University of Pennsylvania, School of Medicine.

Welcome - Norman H. Topping, M.D., Vice-President in Charge of Medical Affairs, University of Pennsylvania.

Introductory Remarks - Russell E. Teague, M.D., M.P.H., Secretary of Health, Commonwealth of Pennsylvania, Harrisburg.

Anthrax in Various Parts of the World - Martin Kaplan, V.M.D., M.P.H., Division of Communicable Disease Services, World Health Organization, Geneva, Switzerland. (Read by Dr. E. J. Witte, Pennsylvania Department of Health)

Appendix A

Epidemiology of Anthrax in the United States - William D. Schrack, Jr., M.D., Dr. P.H., Director, Bureau of Communicable Disease Control, Department of Health, Commonwealth of Pennsylvania, Harrisburg.

Anthrax Studies in Philadelphia - P. W. Purdom, M.S.E., Director of the Division of Environmental Sanitation, City of Philadelphia, Department of Public Health.

Discussion

Intermission

Rapid Isolation and Identification of Bacillus anthracis - Kenneth L. Burdon, Ph.D., Professor of Microbiology, Baylor University, College of Medicine, Houston, Texas.

The Efficacy and Application of Wool Sterilization in the Control of Occupational Anthrax - James H. Steele, D.V.M., Chief, Veterinary Public Health, United States Public Health Services, Atlanta, Georgia.

Appendix B

Industrial Methods and Plant Design as Related to Employee's Health - C.D. Yaffe, M.S., Occupational Health Field Headquarters, U.S. Public Health Service, Cincinnati, Ohio.

Discussion

Intermission

AFTERNOON SESSION

Presiding: C. L. Wilbar, Jr., M.D., Deputy Secretary of Health

Commonwealth of Pennsylvania.

Pathogenesis of Anthrax

Pathogenesis of Cutaneous Anthrax - William J. Cromartie, M.D., University of North Carolina, School of Medicine, Department of Bacteriology and Immunology, Chapel Hill, N. C.

A Possible Case of Inhalation Anthrax - Walter J. Levinshky, M.D., T. G. Anderson, Ph.D., and G. Richardson, M.D., Temple University Hospital and School of Medicine, Department of Medicine, Microbiology, and Pathology, Philadelphia.

Pathogenesis of Inhalation Anthrax - Harry E. Morton, Sc. D., Professor of Bacteriology, University of Pennsylvania, School of Medicine, Philadelphia.

Discussion

Intermission

Treatment

The Effect of Modern Therapy on the Clinical Features and Communicability of Cutaneous Anthrax - Sheldon C. Kravitz, M.D., Baltimore, Md.

Attempt at Preventing Cutaneous Anthrax by Use of a Protective Ointment - Milton Werrin, V.M.D., Chief, Veterinary Public Health Section, Department of Public Health, City of Philadelphia.

Active Immunization with a Soluble Antigen from Cultures of Bacillus anthracis - A. G. Wedum, M.D., Chief, Biological Safety Division, Camp Detrick, Frederick, Md.

Present Day Treatment of Anthrax - Herman Gold, M.D., Chester, Pa.

Medical and Educational Plant Programs - Joseph Shilen, M.D., Director, Bureau of Industrial Hygiene, Department of Health, Commonwealth of Pennsylvania, Harrisburg, Pa.

Discussion

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MORNING SESSION - PRESIDING DR. H. E. MORTON

DR. MORTON: Good morning. Dr. Norman H. Topping, Vice-President in Charge of Medical Affairs, University of Pennsylvania, will welcome you on behalf of the University.

WELCOME

DR. NORMAN H. TOPPING: Thank you, Dr. Morton.

This is a very pleasant occasion this morning when three agencies in the State of Pennsylvania can join together in sponsoring a symposium on anthrax. These three agencies, as you know, are the School of Medicine of the University of Pennsylvania, the Department of Public Health, City of Philadelphia, and the Department of Health of the State of Pennsylvania.

As many of you know, anthrax is a problem in the State of Pennsylvania, a problem that has had a great deal of interest over the years. I think there was a symposium in 1941 on the problem here in Pennsylvania.

There are many questions in the minds of the people who have been interested in anthrax, questions that are of practical significance and, of course, they are also of theoretical importance. One of the problems that I hope someone will discuss today is the rather strange epidemiology at times of anthrax, where there are cases of cutaneous anthrax, and yet at the same time the classical woolsorter's disease doesn't seem to appear. It's quite rare.

In Pennsylvania we have a very considerable industry having to do with the processing of hair and hides, and I think it's mainly in that industry that we see the anthrax that has been reported from Philadelphia and Pennsylvania.

I am sure the conference this morning and this afternoon will be productive. I note that the program is very interesting. On behalf of the University -- and I am sure I can also speak for the City and State Health Departments --

we are very happy that you are here today and we wish you the very best of luck in the seminar that will be conducted.

DR. MORTON: Thank you Dr. Topping. It was originally planned for Dr. Russell E. Teague, Secretary of Health, Commonwealth of Pennsylvania to make some introductory remarks. Members of the State Department of Health are vitally interested in the fact that the State of Pennsylvania leads all other States in the incidence of anthrax in man. Unfortunately, as often happens to a busy man, Dr. Teague has been called out of town. The introductory remarks will be made by Dr. C. L. Wilbar, Jr., Deputy Secretary of Health, Commonwealth of Pennsylvania, Harrisburg, Pa.

INTRODUCTORY REMARKS

DR. C. L. WILBAR, JR.: Dr. Morton, Dr. Topping, ladies and gentlemen: Dr. Teague sends his best wishes for this conference, but unfortunately he had to go to Buffalo for a pre-session meeting of the American Public Health Association.

We in the Health Department are vitally interested in anthrax in this State and particularly in Philadelphia, because of the statistics. There was a conference, as Dr. Topping mentioned, thirteen years ago, but the annual number of cases of anthrax hasn't decreased since then. Maybe more can be done about it through this conference.

Here are just a few figures: In 1945 there were 11 cases reported in Pennsylvania and each year thereafter the annual number was as follows: 15, 17, 17, 14, 25, 26, 14, 14 and this year to date, 12. Last year in the United States, as a whole, 33 cases were reported to the Public Health Service and of the 33 cases, 14 (there is some doubt about one of those) came from Penn-

sylvania. Of that number 9 came from the City of Philadelphia among people working in the hide and wool sorting industry. This year, of the 12 cases that we have had so far, 9 have been from Philadelphia and the other 3 from Delaware County, just outside of the City of Philadelphia.

Interestingly enough, we have practically no anthrax in cattle in the State. The last case was reported in 1950 in cattle and there is only a very occasional case. We do have a death in man due to anthrax from time to time; the last death occurred in 1952. We have had an average of 11 cases of anthrax in man for the past 50 years in the City of Philadelphia. Thus, although anthrax today isn't too serious a disease, the rate in the State of Pennsylvania and in the city of Philadelphia, compared with that of the nation, is not one of which we are proud, and there are many people who feel that it can be appreciably lowered. We hope that as a result of this conference it will be.

DR. MORTON: Thank you Dr. Wilbar. For our next speaker we attempted to obtain Dr. Martin Kaplan, of the World Health Organization, to talk to us about the prevalence of anthrax throughout the world, but at the last moment his plans were changed and he will not return to this country from Switzerland for another month. However, he very kindly submitted his paper, and we have asked his colleague, Dr. Ernest J. Witte, Chief, Division of Veterinary Public Health, Department of Health, Commonwealth of Pennsylvania, to read it for Dr. Kaplan.

I would like to remark now that Dr. Witte has been Dr. Teague's representative and has come to Philadelphia on many occasions and worked very hard in helping to organize this symposium. Dr. Witte.

DR. WITTE: Thank you Dr. Morton. I think Dr. Morton deserves most

of the credit for the work in preparing for this symposium. He was right here in Philadelphia where all of the problems came to him first and he tried to solve them as quickly as he could. I would also like to say that the easiest way to present a paper is to have somebody else write it for you. I have the privilege of reading Dr. Kaplan's paper and because of the time factor I will take certain liberties and not present some of the detailed data which he has in his manuscript. Instead, it will appear in the proceedings of the symposium. I have summarized it, picking out some of the highlights of the paper.

A BRIEF REVIEW OF ANTHRAX PREVALENCE AND EPIDEMIOLOGY

OUTSIDE OF NORTH AMERICA

Martin M. Kaplan, A.B., V.M.D., M.P.H., Chief
Veterinary Public Health Officer WHO, Geneva

A. Prevalence in Man and Animals

Official statistics with respect to anthrax are no exception to the rule that gross under-reporting of communicable diseases is found in most countries. This severe limitation applies to reports of anthrax in both man and animals and should be kept in mind when considering the information submitted in this paper.

Table I contains information abstracted from WHO epidemiological and vital statistics reports of anthrax incidence in man throughout the world in recent years[1]. The list includes only those countries which reported the presence of the disease in 1951 to 1953.

TABLE I

Anthrax Incidence in Man - 1951 to 1953

Country	1951	1952	1953
Africa			
Bechuanaland	1	-	-
Cape Verde Islands	63 (3)	-	-
Egypt	9 (3)	-	6
Eritrea	1	4	8 (2)
French Equatorial Africa	11	-*	-
French West Africa	324 (95)**	-	-
Kenya	1000 (30)	-	-
Libya - Tripolitania	16	7	-
Morocco (Sp.)	11 (1)	-	-
Mozambique	3	-	-
Ruanda-Urundi	224 (9)	-	-
Southern Rhodesia	5	4	2
Spanish West Africa	2	-	-
Tanganyika	368 (18)	-	-
America			
Argentina	110	-	-
British Honduras	12	-	-
Canada (Excl. Yukon & N.-W. Terr.)	(1)	-	-
Chile	223 (21)	278 (21)	-
Colombia	-	-	36
Costa Rica	4	-	-
Ecuador	5	-	-
El Salvador	17	4	-
Guatemala	38	31 (2)	-
Haiti	11 (1)	-	-
Mexico	172	114	-
Paraguay	31 (1)	-	-
Peru	33	-	-
Puerto Rico	1	-	-
United States	60 (3)	42	33
Uruguay	61 (2)	87	102
Venezuela	155 (1)	130 (1)	-
Asia			
Ceylon	282	-	-
Cyprus	-	-	1
Iraq	281 (1)	281	196 (1)
Japan	2	1 (1)	3 (1)
Jordan	1	-	-
Portuguese India	1	-	-

TABLE I (Continued).

Country	1951	1952	1953
Syria	1	-	-
Thailand	(7)	-	-
Timor	1	-	-
Europe			
Austria	1	-	-
Belgium	8	8	7
France	(2)	-	-
Germany - Federal Republic	25 (2)	20	7
Greece	135 (1)	164 (6)	132
Italy	1058 (8)	1364	931
Norway	-	-	2
Portugal - Mainland	1697 (22)	-	-
Azores & Madeira Islands	2	-	-
Spain	1312	904 (20)	1054 (7)
Turkey	1239 (32)	1666 (30)	-
U.K. - England and Wales	(1)	(2)	-
Scotland	-	(1)	-
Northern Ireland	4	-	4
Yugoslavia	1023 (33)	1265 (24)	894 (9)
Oceania			
Australia	-	-	1
Papua and New Guinea (Austr.)	-	3	-

* - No Cases reported.
** () Deaths reported.

The blank spaces in Table I are as revealing as the figures given. For example, the high figures shown for such territories in Africa as French West Africa, Kenya, Ruanda-Urundi, and Tanganyika indicate superior reporting in these areas and probably reflect the situation in other countries of the region, even though these latter countries report no or little disease. The absence of Iran and Pakistan in the Asian group of countries listed is a good illustration of the limitations of official reports, since anthrax in animals in these countries is highly enzootic* and anthrax in human beings is also known to be common but unreported. The correlation of a relatively high incidence of human infection with a highly enzootic status of the disease in the animal population is reflected in the figures of several Mediterranean countries, notably Portugal, Spain, Italy, Turkey, and Yugoslavia. Greece can well be added to this category although the figure given in the Table is relatively much less than the neighbouring countries. No information is included from Eastern European countries, the Soviet Union and China. Anthrax in man and animals is known to occur

*In 1945, for example, 1 million out of the 15 million sheep in Iran were reported to have died of anthrax[2].

frequently in these areas but the extent is unknown.

Useful information on the general situation with respect to anthrax in many countries is given by Simmons, Whayne, Anderson, and Horack in their volumes on "Global Epidemiology". The following data are taken from this source[3].

AFRICA

Algeria - Enzootic among the sheep, but human cases are seldom reported.

Anglo-Egyptian Sudan - Occasional cases reported.

Angola - Enzootic among the cattle and the sheep. Occasional human cases occur as the result of contact, or the ingestion of meat from infected animals.

Basutoland - Occurs sporadically. Human cases result both from contact with infected animals and from the consumption of infected meat.

Canary Islands - Human cases observed sporadically.

Egypt - Human infections occur sporadically.

French Equatorial Africa - Enzootic among the livestock, and human infections are probably numerous.

French West Africa - Outbreaks in humans occur sporadically in association with epizootics among the livestock. Infection often results from the consumption of the flesh of diseased animals. Acute and chronic infections caused by Balantidium coli are observed frequently in Guinea and Niger.

Gold Coast - Reported occasionally.

Guinea, Portuguese - Enzootic among the livestock.

Kenya - Common among the natives on the reserves. The disease is prevalent in the cattle, and frequently human infections are acquired not only by contact but through the consumption of infected meat. From 600 to 800 known cases are reported each year. The fatality rates average from 2 to 5 per cent.

Human infections are numerous and may be transmitted through contact or through the intestinal tract. In some tribes infection may result from the use of the fat of infected animals for oiling the sking.

Libya - Sporadic cases in humans.

Madagascar and Comores archipelago - Enzootic among the livestock. Roughly, two million animals are inoculated each year with anti-anthrax vaccine. The extent of human infection is uncertain, but incidental cases undoubtedly occur.

Morocco - Sometimes epizootic among the sheep and the goats. Occasional human cases result from contact with infected animals.

Mozambique - A few foci have been established in the southern provinces, and human cases are reported sporadically. In the tribal areas they may result from the consumption of meat from infected animals.

Nigeria - Occasional human cases are observed due to the consumption of meat from infected animals.

Rhodesia, Northern - Enzootic among the cattle, and infections sometimes occur among the natives as the result of eating meat from infected carcasses. Human infections are frequent. The majority follow the consumption of meat from infected animals, but some may result from contact.

Rhodesia, Southern - Sporadic cases are encountered among the Bantu, often as the result of the consumption of the meat from infected animals.

Ruanda Urundi - Present among the herds, and human infections occur from time to time.

Somaliland, British - Infections are encountered from time to time.

South West Africa - Human cases are frequent in the native areas, particularly in Ovamboland, due largely to the consumption of meat from infected animals. Contact infections are occasionally recorded among the Europeans.

Swaziland - Occasional human cases are reported.

Tanganyika - Between 50 and 100 human cases are reported almost every year from various sections of the country. As in other areas, infections among primitive tribes are most frequently attributed to the consumption of infected meat.

Uganda - Human cases are reported from time to time, in which infection follows the consumption of meat from infected animals.

Union of South Africa - Human cases are encountered frequently in the cattle-and sheep-raising areas.

ASIA

Afghanistan - Enzootic among the livestock, and human infections occasionally result from close contact with infected animals.

China - Reported from many areas of China; namely, Hankow in the province of Hupeh, Tientsin in the province of Hopeh, Newchwang in the province of Liaoning in Manchuria, Chinkiang and Shanghai in the province of Kiangsu, and Chengtu in the province of Szechwan. In most cases the disease occurs among persons who handle bristles, horse-hair, and hides. Cases in

which anthrax questionably was present have been reported from the southern part of China, but in most cases the disease occurs in northern China.

Cyprus - Enzootic among the sheep, and human infections are sometimes observed.

French Indo-China - Reported from all parts of French Indo-China. Apparently, it was most prevalent in the southern part of Annam, where it caused from 40 to 96 deaths a year.

Iran - Enzootic among the livestock, and human infections are frequent, particularly in the rural areas. The majority are skin infections, acquired through contact or by the handling of wool, hides or meats from infected animals.

Iraq - Prevalent among the sheep. From 130 to 225 human cases are reported annually among persons in contact with infected animals, or among individuals working with hides or wool.

Israel - Enzootic among the local sheep, and human infections are encountered occasionally.

Japan - A few cases are reported each year.

Jordan - Enzootic among the sheep, and human cases are sometimes reported.

Korea - Reported, but is infrequent.

Kuwait - Although enzootic among the sheep, few cases of human infections are seen.

Lebanon - Enzootic among the sheep, and human infections occur occasionally.

Netherlands East Indies - Probably occurred in all the islands of the region. Epidemics of the disease among human beings broke out occasionally, usually preceded and accompanied by an epizootic among the carabaos or water buffaloes (Bubalus bubalus).

Saudi Arabia - Enzootic among the sheep in many areas, and human cases probably occur from time to time, although few have been recorded by medical observers.

Syria - Enzootic among the sheep, and human infections sometimes occur in the agricultural areas.

Thailand - Forty-three cases, with 11 deaths, were reported from Thailand in 1934.

Turkey - Prevalent among the sheep and other animals, and human infections are numerous in the agricultural areas. No instances of industrially acquired infection have yet been recorded. An average of 1,493 human cases was reported annually in 1946-50, with fatality rates of 2.5 to 5.8 per cent. The mass immunization of sheep and other susceptible livestock is being promoted by the veterinary division of the Ministry of Agriculture. All anthrax vaccines are prepared at the Etlik Institute, near Ankara.

Yemen - Not reported, and information regarding its presence is lacking.

OCEANIA

New Zealand - A few cases are reported annually.

B. Epidemiology

The scope of this paper does not embrace the epidemology of anthrax in its broad sense. A few observations, however, might be of interest.

The ruminant is the most important reservoir of anthrax. Other animals, particularly horses and swine, are commonly affected but infection of these animals is usually secondary in important to the ruminant. In the Eastern Hemisphere sheep are, by far, the animal most commonly infected, and next in order are cattle. In heavily infected countries, even in relatively underdeveloped areas, the disease is well known to all livestock owners since a failure to vaccinate their herds periodically often results in economic catastrophe.

Despite general awareness of the disease amongst shepherds, anthrax often strikes a flock without warning and the peracute form of the disease is frequently not recognized. The first sign may be the sudden toppling over and death of an animal, with no other visible signs. Since such an occurrence is seen also in the uniformly heavily parasitized animals of these areas, the carcass may be used for food, or left to rot in the field after skinning. This is the usual history of anthrax outbreaks in both man and animals in underdeveloped rural areas.

Anthrax in man usually results from cutaneous infection or by ingestion

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Anthrax in man usually results from cutaneous infection or by ingestion

of contaminated meat. Local skin infections are the form generally seen in North America and western Europe, as elsewhere wherever anthrax exists in animals. Because of the paucity of published reports, however, it is not ordinarily realized that intestinal anthrax is also quite common, particularly in underdeveloped countries. Virtual epidemics of intestinal anthrax occur in highly enzootic areas of these countries. Knowledge of these epidemics is gained often by chance in discussions with local medical authorities or, more likely, with veterinary officials who deal with anthrax epizootics amongst the animal populations.* The poverty and ignorance of the rural dweller in these areas, the infrequent luxury of meat, and often the practice of eating raw or insufficiently cooked meat (particularly in Africa) contribute to epidemics of intestinal anthrax.

One of the consequences of heavily infected animal populations is the risk to importing countries of animal products from infected areas. This problem concerns most European countries, as well as the U.S.[4]. For measures taken by various countries with respect to meat and bone meal the reader is referred to a consideration of the subject by the International Office of Epizootics[5]. For other animal products such as wool, hides, etc., the unique Government Wool Disinfection Station at Liverpool is worthy of special mention[6]. The continued work on disinfection of hides and factory effluents, however, reveal the unsatisfactory state of affairs, from a practical point of view, for other countries[7].

Finally, it is of interest to mention a study recently made by Minett[8] on the annual and seasonal incidence of anthrax in livestock of various countries. He analyzed the seasonal incidence of animal anthrax in several countries to determine if the climate exerted any influence on the distribution of outbreaks,

* A good description of an epidemic of human intestinal anthrax appeared in the Philippines Bureau of Animal Industry Gazette, March, 1932, Vol. II, No. 3. This article was called to the attention of the author by Dr. James H. Steele, another speaker at this Symposium.

particularly through its effect on sporulation. While many other factors apart from climate were found to be operative, hot climates favoured sporulation and a resultant high incidence rate. Minett's study is a synthesis of much scattered information not readily available to students of anthrax epidemiology.

Summary

Anthrax is found in practically all parts of the world with the heaviest areas of infection in the Mediterranean region, Africa, and Asia. Official reporting of anthrax incidence in man and animals is very deficient. A few epidemiological facets of the disease, particularly in reference to rural areas of underdeveloped countries, are briefly discussed.

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Dr. Morton: Thank you, Dr. Witte.

APPENDIX A

THE LAST ANTHRAX OUTBREAK IN LA UNION

LUZON, PHILIPPINE ISLANDS

Estefano C. Farinas, D.V.M.

(Note: The writer was sent by the Bureau of Animal Industry to the barrio of Sinapangan, Bangar, La Union, on March 3, 1932, to investigate the reported cases of anthrax in that place. His full report which follows was supplied for these proceedings by Dr. James H. Steele.)

HISTORY

On February 14, 1932, a caraboa owned by one Andres Maala of Sinanpangan, Bangar, La Union, died. According to Maala, this carabqa was used to plow his farm on February 13, 1932, and the next morning, he noticed that it ate sparingly and at noon refused food altogether. In the afternoon, the animal was still more indisposed and listless; then it lay down from which position it was not able to move despite the efforts of the owner to make it stand up. At about 6:30 p.m., the animal was in the agonal stage and Andres Maala notified the "teniente del barrio," Valentin la Cuadra, who went to see it, but when he arrived, the animal was already dead. The owner could not tell the symptoms manifested by the animal other than what have already been stated despite the writer's suggestive questions.

Valentin la Cuadra, the barrio lieutenant, decided to have the animal buried. He ordered Andres to call for some men to help bury the carcass and the former went to summon the second barrio lieutenant. One Sixto Miliano began digging the hole. Andres arrived at the place where the carcass was to be buried, with Isidro Maala, Miguel Dingle, Severo Millares, and Catalino Dingle. The teniente arrived with Eugenio Millares. Valentin then told Andres, at the suggestion of Isidro Maala, that some more men were needed to drag the caraboa to the hole. So Andres went to call Apolonio

Mico and Gaspar Mico; and Valentin called Juan and Gregorio Millano. Upon their arrival, they found the caraboa already quartered and several persons engaged in a merry scramble for the meat. Andres Maala stated that only the hide was buried, the meat and other parts were used for food. The horns were recovered; one from the owner, Andres, and the other from Valentin la Cuadra, the barrio lieutenant. Those horns were submitted to the Bureau of Animal Industry research laboratory for analysis.

Until now, no criminal action has been filed against these men, but the Constabulary is investigating and gathering the sworn statements of the men responsible.

In the barrio of Sinapangan, there are about 70 houses and 514 inhabitants, of which 261 are men and 253 are women. Seventeen persons died after eating the meat of the carabao that died on February 14, 1932. There were eight persons in the convalescent period, one of whom was considered as a contact case. About 20 houses were involved.

The deceased were:

Name	Date of death
1. Isidro Maala	February 20, 1932
2. Sebastian Mibalo	" 21, "
3. Maria Maala	" 22, "
4. Timoteo Cuntawi	" 22, "
5. Emitoria Maala	" 23, "
6. Alfredo Maala	" 23, "
7. Simeon la Cuadra	" 23, "
8. Catalino Dingle	" 23, "
9. Benito Maala	" 23, "
10. Miguel Dingle	" 23, "
11. Severo Millares	" 23, "
12. Petra Catalina Maala	" 24, "
13. Cristina Mibalo	" 24, "
14. Juanita Maala	" 24, "
15. Jorge Mendoza	" 25, "
16. Segundo Mendoza	" 29, "
17. Alejandra Maala	March 1, "

Six out of those people, namely; Cristina Mibalo, mother, and Maria Maala, Emeteria Maala, Alfredo Maala, Jacinto Maala, and Alejandra Maala, children, belonged to the same family.

The incubation period of the disease was from three to five days and its duration varied from a few hours to a few days.

The families that ate the meat of the infected carabao, and which so far, have not contracted the disease were those of:

1. Cipriano Lopez
2. Maximo Pascua
3. Casimiro Pascua
4. Regino Mibalo
5. Carlos Sibayan
6. Valentin la Cuadra
7. Rufina Maala
8. Andres Maala
9. Engracio Miliano
10. Juanario Millares

Since the carabao was very big and fat (it was the only carabao that Andres Maala had and was consequently very well taken care of) I estimated that more than one-half of the whole barrio of Sinapangan, involving no less than 30 houses and 250 people had shared in the carcass. Dogs and pigs also must have eaten small pieces of the meat, or meat washings. But no case among dogs nor among large animals was discovered.

A young boar owned by Marcela Millares was reported to have died from the bites of a sow, but it is possible that it might have died after eating a part of the infected meat.

A certain young woman by the name of Maria Dingle, sister of one of the victims, Catalino Dingle, was questioned by the writer. She said that, one morning, after the burial of her brother, Catalino, while trying to look for some tomatoes for breakfast, she came across a piece of "tapa" in a bamboo basket ("Upit" in the dialect). Her sister-in-law forbade her to eat the meat, saying that it was the cause of the death of her husband. Maria told her sister-in-law to throw the meat away, and it was then eaten by a

hog. Nothing definite could be gathered after this but in the writer's opinion, the young boar died after having consumed the infected meat.

A survey of the animals in the barrio disclosed the fact that all carabaos, cattle, and horses were pastured in the lowlands after the rice harvest, and a recent branding of large cattle in the place made possible a check-up of the animals there. No animal became sick or died in the locality during the writer's presence in Bangar. An inquiry as to the number of animals that died previously revealed that one animal belonging to Claro Maala bearing certificate Number 6770524 was castrated on January 30, 1932, and died on January 31, 1932. The carcass of this animal was clandestinely quartered by the late Isidoro Maala as leader, and shared by Catalino Dingle, Claro Maala, Engracio Miliano, Valentin la Curra, Marcelo Maala (1) Marcelo Maala (2) Pascual Monis, Pedro Monis, Simeon la Cuadra, Maximo Maala and eaten by them and their families without any untoward effects. It is a fact that people in many parts of the Islands eat the meat of dead animals without feeling any bad effects, and with regard to the people of Bangar this is not their first experience of an "infection" of this nature. Balbina Padilla, 63, living in the poblacion of Bangar declared that when she was only 12 years old, a carabao belonging to a certain Capitan Bernardo Mangibin suddenly died in Pao, then part of Sinapangan, which is now called Rissing. It was eaten by the tenants of Capitan Bernardo. Of those tenants, nine died. This was corroborated by Apolinario Ramos, 79, a resident of the barrio of Rissing, who even remembered the names of three of the victims, who were Clemencia Pascua, Diego Labastera and one Magpale.

In this connection the writer also inquired into the death of the other animals. He discovered that dogs had died of rabies after the planting

season; the fowls were actually suffering from avian pest; one horse in the municipal jail in Balaoan was examined and was at first believed to have died from hemorrhagic septicemia but was later on found to have died from anthrax according to the laboratory findings on the specimens taken from the animal; one carabao 30 years old, belonging to Apolonia Ufano in San Fernando, La Union, died about two weeks before, apparently from old age and debility. The appetite of this carabao was never impaired according to Vicente Jimenez, who I questioned.

With regard to the human cases of the disease the following are the persons who were found convalescing:

1. Ildefonsa Rodriguez, married, with carbuncle, at the back palm at the base of the middle finger. She was the one who prepared the meat for the family; and confessed that she ate the meat of the infected carabao.

2. Ignacio Mibalo, married, with carbuncle on the right thigh. He had participated in the partition of the carcass and had prepared the meat for the family. Confessed he ate some of the meat from the dead carabao.

3. Marcelo Daos, married, with carbuncle on the forearm. Took part in the cutting of the meat and ate some of it.

4. Dionisio Dingle, married, with carbuncle on the small finger. Confessed that he had not touched any of the meat but that the caretaker of his deceased cousins, Miguel and Catalino Dingle, had skin lesions.

5. Tomas Granada, married, had no carbuncle but an enlargement of the lymph glands of the arm. He suffered dizziness and headache. Confessed that he had handled, prepared, and eaten the meat of the dead carabao.

6. Gregorio Miliano, married, had enlargement of the right axillary

lymph gland. Said that he had visited the victims.

7. Pio Maala, a boy of seven years, member of the family where six persons died. Ate the meat, had fever, headache and abdominal pains.

8. Francisco Mendoza, married, had fever, headache and enlargement of left axillary lymph gland. Denied having been in contact with any of the victims who had eaten or handled the infected meat.

All of these persons were apparently convalescing at the time they were observed. Specimens were taken from the carbuncles of Ignacio Mibalo and Marcelo Daos, but on examination the stained preparations made from them proved negative. Dried blood obtained from the carbuncles was preserved for inoculation into laboratory animals at Pandacan. The exhumation of the carcass was suggested by the representatives of the Philippine Health Service, but the writer did not agree to the idea fearing the infection of the laborers.

The writer succeeded in recovering the horns, hoping that their examination might reveal the cause of the infection. He then believed that if the disease was anthrax its germs might be found in the vascular part of the horns or on the surface.

SYMPTOMS

An inquiry into the symptoms and lesions manifested by the victims revealed the following:

1. It took about three days for the symptoms to appear after the patient had handled or eaten the meat.

2. The duration varied from a few hours to a few days.

3. The intestinal form of the disease manifested itself by abdominal pains, fever, dizzines, and headache. The feces in some cases were coated

with tarry blood. Constipation was common among the victims.

4. The cutaneous form manifested itself in the form of one or two carbuncles with vesicles. The swellings were not painful at first, but they became so when the inflammations acquired the size of large tumefactions. The swelling and the skin around it were red, and the tumor was firm or hard. The arms were the parts mostly involved and the hard malignant edema extended to the base of the neck, breast, and side adjacent to the affected organ. There was no pus.

5. Chills preceded the fever which lasted on the average from one to one and a half days. Later, the fever subsided and subnormal temperature followed. In the fatal cases, there was weakness, then extreme prostration followed by coma and chilling of the extremities which gradually spread to the center of the body until death.

6. In the non-fatal cases, some of the above symptoms occurred in a lesser degree.

LESIONS

1. Carbuncles of different sizes appeared in five of the 17 who died and in four of the convalescents. They contained blisters or continuous vesicles (not multiple) about the size of a ten or a twenty centavo piece and had no pus. There were lymph gland enlargements in the arm or axillary regions.

2. No blood was observed at the natural openings after death.

3. No internal lesions were found as no autopsy apparently was made. The step taken by the Philippine Health Service was to treat the disease as anthrax and to make thorough disinfections, quarantine the houses of the patients, treat the carbunciles with phenolic acit cautery and give anti-anthrax

serum intramuscular injection to each patient.

On the part of the Bureau of Animal Industry, the imposition of a restriction on the movements in and out of the infected barrio was advised. Further scouting work to discover other cases among animals was planned.

ACKNOWLEDGEMENT

The writer wishes to acknowledge with thanks the cooperation extended to him by Mr. Francisco Mortera, municipal president of Bangar, La Union, Drs. Coronel and Javier and Miss Nebres, of the Philippine Health Service, and the 2 representatives of the Philippine Constabulary in making this investigation.

FROM: BUREAU OF ANIMAL INDUSTRY GAZETTE, 3/32 - Vol. II #3

DR. MORTON: I am very happy to announce the next speaker, Dr. William D. Schrack, Jr., of the Bureau of Communicable Disease Control of the Department of Health in Harrisburg, one of our former students, who will speak on "Epidemiology of Anthrax in the United States." Dr. Schrack.

EPIDEMIOLOGY OF ANTHRAX IN THE UNITED STATES

William D. Schrack, Jr., M.D., M.P.H., Director,
Bureau of Communicable Disease Control,
Department of Health, Commonwealth of Pennsylvania,
Harrisburg, Pa.

The program today is very comprehensive and, as specific aspects of the subject have been assigned to different speakers, in order to avoid repetition or duplication, I shall confine my remarks to a few very general observations concerning the sources of infection as found in the United States. I know all of you are familiar with the epidemiological study of industrial anthrax by Doctors Wolff and Heimann (1) covering the 31-year period from 1919 to 1949. More recently Doctor Steele (2), who will address you a little later this morning, has presented this subject in last year's June number of Public Health Reports.

For purposes of analysis and study, anthrax cases are classified according to the type of occupation of the worker who develops the disease. On the basis of this description, cases are classified either as agricultural or industrial. Between 1919 and 1938 slightly more than one-half of the cases which were reported were classified as industrial, while approximately 30% were agricultural. The sources of the remaining approximately 20% of the cases were either "unknown" or classified as "other". From 1939 to 1949, 80% of the cases were industrial; 14 1/2 % agricultural; and in only 5 1/2 % were the sources classified as "unknown" or "other".

During the 18 years from 1934 until the end of 1951, 1229 cases of anthrax in man were reported in the United States. Seventy per cent of these occurred in the New England and Middle Atlantic States. Of these 859 cases in this part of the country, only 12 were agricultural.

During this 18-year period, 326 of the cases in the northeastern part of the United States occurred in Pennsylvania. All but four of these were industrial. Thus, in Pennsylvania there occurred more than one quarter of all cases of anthrax in man in the United States during the 18-year period from 1934 to 1951.

AGRICULTURAL ANTHRAX

The areas in which epizootics had occurred in the United States before 1951 were generally speaking:

Lower Mississippi Valley

Certain areas in California

Texas

Missouri

Nebraska

South Dakota

The extensive outbreaks of anthrax in swine, chiefly in the mid-west, in 1952 were foreshadowed by the occurrence in 1951 of outbreaks in animals in 15 states and 51 counties which had had no history of the disease prior to this time. The epidemiological evidence that the outbreaks in 1951 and 1952 in 6 of the states -- Illinois, Ohio, Indiana, Michigan, Missouri, and Wisconsin -- were due to contaminated bone meal feeding supplement was substantiated by laboratory findings. In these 6 states 356 farms were involved. Throughout the country cases in swine were reported from 935 farms in 308 counties in 15 states. There were no cases in human beings on any of these farms. Early investigation of the outbreaks and extensive public health education most certainly played a part in preventing the occurrence of cases in man.

INDUSTRIAL ANTHRAX

About 90% of all cases of industrial anthrax are found to occur in workers exposed either to carpet wools or to goat hair or goat skins imported from areas of the world where anthrax is prevalent. Almost without exception, industrial cases of anthrax are cutaneous. Modern therapy has reduced the mortality rate from industrial cutaneous anthrax from about 20 per 100 cases to almost zero. Inasmuch as there is widespread distribution of spores in manufacturing plants processing these materials, it is difficult to understand why cases of pulmonary anthrax are so rare.

I thought you might be interested in the earliest reference we could find of official recognition of anthrax control in Pennsylvania. In the Second

Annual Report of the State Board of Health for 1886 several pages are devoted to the problem presented by shipment of 4910 bales of Japanese Rags. An excerpt from the committee's report reads as follows:

"Lazaretto Committee report: recommend that, unless they (the rags) be submitted to some process which in the opinion of the Board will render innocuous any disease-bearing germs or spores they may contain, the admission of these rags in Philadelphia be refused.

"November 5. RESOLVED, That the bales of rags imported upon the vessel 'Lucy A Nickles', consisting of 4,910 bales, be permitted to be landed and be stored in Fitzpatrick & Pemberton's stores; that they shall not be opened or removed from said storehouses while they remain in Philadelphia, without the consent of the Board of Health, and that the consignees give their bond with surety or sureties, in the sum of five thousand ($5,000) dollars to the health officer to comply with the above condition."

I would like to pay tribute to the work of the Committee on Anthrax of the American Public Health Association, the Chairman of which was Doctor Henry Field Smythe, who labored untiringly for many years for better reporting and investigation of the sources of infection of all cases of anthrax. I believe all of you will agree that, to a large extent, the recommendations made by Doctor Smythe's Committee were sound and have stood the test of time. That there are unanswered questions concerning the control of anthrax is self-evident -- or we would not be here at this meeting today.

References

1. Wolff, Arthur H., and Heimann, Harry: 1951 Industrial Anthrax in the United States, Am. J. Hyg., 53, 80-109.

2. Steele, James H., and Helvig, Raymond, J.: 1953 Anthrax in the United States, Public Health Reports, 68, 616-623.

DR. MORTON: Thank you, Dr. Schrack. Now we are gradually getting the attention focused to the situation in Philadelphia. The next paper deals with anthrax studies in Philadelphia by Mr. Purdom, who is Director of the Division of Environmental Sanitation of the City of Philadelphia Department of Public Health. Mr. Purdom.

ANTHRAX STUDIES IN PHILADELPHIA

P. W. Purdom, M.S.E., Director, Division of Air Pollution Control and Environmental Sanitation, and Milton Werrin, V.M.D., Chief, Public Health Veterinary Medicine Section, City of Philadelphia, Department of Public Health, Philadelphia, Pa.

Philadelphia has been a city of many firsts. For years this city has led in varied activities such as industrial development, scientific achievement, and in the number of single family dwellings. It also has the unenviable distinction of being the first city in the United States in which a recorded case of human anthrax was decribed. It seems that the disease broke out in cattle grazing on the town commons (where the City Hall is now located) and persons skinning these animals were infected. This undistinguished event occurred in 1834. Since then anthrax or murrain, as the disease was then called, has been in our midst. We are not happy about it, but Philadelphia at the present time possesses the highest incidence of this disease in this country. High or low production years, depressions, wars, strikes, and relocation of the in-

volved industries seem to make little difference in the morbidity rate. A breakdown by decades would show the following:

Period	Cases Reported	Fatalities Registered
1905 - 1914	80	13
1915 - 1924	116	21
1925 - 1934	88	10
1935 - 1944	107	5
1945 - 1954	112	6

The relationship between number of cases and fatalities show the effect of the antibiotics and sulfonamides in the lowering of the fatality rate from this disease. The decade of 1915 - 1924 with its 116 cases and 21 deaths and the comparable decade of 1945 - 1954 with its 112 cases and only 6 fatal cases shows conclusively the value of these agents. Anthrax must still be classified as a dangerous industrial disease, as any clinician will testify even though he has the help of the antibiotics.

Anthrax in Philadelphia has been and still is primarily an industrial disease. For many years this city has been the leading textile and tanning center of this country. Because of this a large majority of our cases have occurred in these establishments that handle and process wool, hair, and hides. A study of the records from 1948 to the present time was chosen to present certain facts concerning this disease because complete epidemiological records were available only from that date. During this 7 year period 72 cases with 6 fatalities were recorded. The following chart indicates the type of establishment in which anthrax cases have occurred during this period.

Type Establishment	Cases
Wool Processing	34
Hair "	24
Tanning (Leather)	7
Other	7

During the last 4 years (1951 - 54 to date) the incidence of the disease has changed so that at the present time the hair processing plants have produced more cases of anthrax (20) than the wool processors (17). The same period produced only 3 cases in the leather tanning plants. The probable reason for this situation has been the gradual relocation of wool plants to other locations outside of the city limits. The hair processing business has remained stable with no loss of plants, and the employment rate has been unchanged during this period.

The number of cases occurring in the leather industry will probably drop to even lower levels as very few plants are now in operation in this city. Recently one of the largest tanners moved its plant to another state with the loss of over 300 workers at risk in Philadelphia. But in spite of these losses the plants that have remained are still supplying the same number of cases as in the past when more plants were operating in this city.

The materials handled by these plants come from the far corners of the world. During the last 7 years not one case of anthrax could be attributed to wool, hair or hides produced within the continental limits of the United States. Every case investigated showed the materials processed were from anthrax endemic areas. Some of the countries from which infected materials have given rise to cases in this city are China, India, Pakistan, Iran, Arabia, North Africa, Italy, and Argentina.

The control of anthrax by more advanced programs of veterinary and sanitary sciences in these distant lands will undoubtedly have its full effect on the number of cases that constantly occur in Philadelphia. An agency such as the World Health Organization and the Food and Agriculture Organization can be of great instrumental value in the control of this disease. They employ experts, educational staffs with materials, and some funds to aid any country where the disease is present and where there is a sincere desire to eradicate this infection.

Not only are the workers in the tanning and textile plants endangered by infective material but cases occur in humans from the time the materials are unloaded from a ship and taken to a processing plant. Two truckers became infected after loading their truck with hides and hair and hauling them to a factory. There probably are cases where the seamen have contracted the disease but to this date none have been reported to the Philadelphia health authorities. We have found cases in persons employed to service the machinery through which contaminated materials had passed. Even after the machinery has been removed and discarded it still can produce infection.

A number of cases have involved scrap metal workers whose jobs consisted of breaking up this machinery. There is strong evidence that the air itself can become polluted to such a degree as to cause anthrax. In this connection a case was investigated involving a housekeeper who contracted anthrax by the inhalation of the infective organism. She did not have any contact with infective material in her home or in the homes of her friends and relatives. The only possible source of the infection was a waste wool and hair plant located about 50 yards from her home. She contracted the pulmonary form of the disease and died. Another case also involved a housewife

whose only contact with infective material was her husband who worked in a wool scouring plant. Two cases were investigated in which no source of infection could be found. One involved a child of 3 who died of pulmonary anthrax - the other case was an iceman.

In any of the processing plants no group of workers can be said to be entirely safe from contracting the infection; the only exception being the office workers. No cases have been found in this class of employees. The type of work a person performs in these plants seems to have some effect on the infection rate. According to records persons employed in the spinning department of hair processing plants are more often infected than in any other type of occupation. Fifteen spinners have become ill with anthrax during the last 7 years. In one of our hair plants reporting 20 cases, 11 occurred in spinners. The group showing the next largest number of cases were pickers. Seven pickers have contracted anthrax in the last 7 years.

Every department of wool, hair, and tannery plants have had cases during the above period of this study. As there are 24 different types of work listed, the number of cases is very small for each type. The exception being the spinners and the picker plant operators.

Skin lesions form 97% of our anthrax cases. The most usual sites for cutaneous lesions are the arms, hands, face, neck, and chest in the order named. Our records show that forearm and hand cases amounted to 35 cases or 48.6%. Cases involving the face and neck showed 24 cases or 35%, those lesions on the chest amonted to 8 cases or 11% and other parts of the body 5 cases or 7%. The above statements bear out the rule that anthrax attacks most frequently those parts of the body that are unprotected by clothing or gloves. As most of the workers in these plants wear shirts

and blouses that are sleeveless, and as most of the work must be performed without gloves (especially the spinners), one can readily see the reason for the above areas being most often involved.

Most of the operations taking place in a hair and wool establishment are performed in a dusty atmosphere with discernible strands of wool and hair floating about. This dusty, hair laden environment leads to a greater amount of scratching and itching with the resultant possibility of introducing the organism into the skin. The cuts, bruises, and small tears produced by encounters with metal parts of machinery and the more overlooked factor of actual embedment of hair and wool under the skin are all factors in the cause of this disease among employees in our plants. The removal of hair splinters is almost a universal practice in one plant. They are removed by means of a non-sterile needle and the small wound produced is never covered or treated. A number of anthrax lesions have developed at these sites.

Untreated or unprotected tears and scratches produce more cases of anthrax than probably any other cause. In only one case could it be shown that an insect bite produced an anthrax lesion. The worker was a master dyer in a wool processing mill who definitely remembers being bitten by a flea, the lesion appearing a few days later at the site of the bite. A contributing cause for accidents to the exposed skin is the poor lighting. In only one plant where a case of anthrax developed was adequate lighting provided.

Further analysis of our case records has shown a definite seasonal occurrence of anthrax in our industrial workers. During the last 7 years the following variations were found.

Time of Year	Cases	Percent
Jan. 1 to March 31	20	27.6
April 1 to June 30	25	34.7
July 1 to Sept. 30	9	12.5
Oct. 1 to Dec. 31	18	25.0

A number of factors may contribute to the lowered incidence during the July to September period including better ventilation of the plants because of open windows, greater frequency of bathing by the workers and a possibility of better lighting due to the greater amount of sunlight present with an attendant decrease in minor accidents to the skin.

The factors which operate to produce a lowered incidence of the disease during the summer months should be further investigated. However, it should be stated that workers do receive vacations during this period and also the wool and tanning industries undergo a seasonal decrease in production.

In the case of the hair plants the summer months show a slight drop in production but not as great as in the wool processing plants. Whether the above fact would produce a three-fold drop in comparison with the spring months or a two-fold decrease compared with the fourth quarter of the year is a question that will have to be studied further before it can be ansered.

In many disease conditions immunity is sometimes achieved by receiving small amounts of the infective agent. In the case of anthrax this situation apparently does not occur. Workers do not appear to acquire any immunity no matter how long they work in the presence of infective material. There is a wide variation in the length of time an employee works in a plant and the time he becomes an anthrax patient. The shortest period of time between employment and acquiring the disease has been two weeks. The longest

interval has been 24 years. Unfortunately our records are not complete in this matter of length of time of employment, but in 42 cases where this information is available 21 workers contracted the disease within three years. Sixteen cases developed in workers whose employment range was from 8 to 24 years.

The adoption of the Philadelphia Home Rule Charter, April, 1951, empowered the Department of Public Health to enforce and administer rules and regulations dealing with health hazards in the pursuit of occupations effecting the public health. With the reorganization of the Department of Public Health and the creation of the Division of Environmental Sanitation ground work was laid for further attacks on this occupational disease. A section on Veterinary Public Health and Industrial Hygiene was installed. Further research in the control of and protection against this disease has been entrusted to these sections.

Some of the research problems that are contemplated in the near future consist of the part steam sterilization plays in the prevention of anthrax. A bacteriological study of the organism itself in the raw material and in the entire environment in which the workers find themselves is being contemplated. Also there will be investigations made of the organisms found on the exposed surfaces of the skin of those workers. These sections will also work with U. S. Public Health Service officials in a vaccination program of the workers, if and when a program is to be undertaken in this city.

DR. MORTON: Thank you, Mr. Purdom. Since the last three papers deal with a common aspect of anthrax, they will now be open for discussion. We would like to remind the participants of the symposium that we would enjoy a good deal of discussion from the floor. If you have any remarks to make, or

lengthy questions to ask, please come forward, or else speak very distinctly, so the reporter may take down your remarks. We intend to include the discussion in the proceedings of the symposium as well as the original papers.

Are there any comments about the first three papers?

DR. STEELE: I would like to take the opportunity to enlarge on Dr. Kaplan's short statement about the intestinal anthrax in the Philippine Islands. This report, a copy of which will be supplied for an appendix to Dr. Kaplan's paper, came to us just a few years ago, and, in summary, the report was that a carabao, that was of very good flesh, had died. An agriculture inspector in the area had advised that the animal be buried. The community was short of meat and had been short of meat for a good many months. The animal was dug up that night, the hide removed, the flesh distributed in this small community to approximately 132 persons. Among those who came in contact with the carcass, there were 25 known cases of anthrax with about 17 deaths, I believe.

DR. MORTON: Dr. Mudd, you are lecturing this afternoon to the medical students on epidemiology. Do you have any comments to make?

DR. MUDD: I have some very good information to pass on to them, but I have nothing to add myself.

DR. MORTON: I would like to ask Mr. Purdom a question. He mentioned that most of the cases of anthrax infection in the workers occurred in the spinners and pickers. Does something happen in the processing of the wool beyond those stages which destroys the spores?

MR. PURDOM: I would suspect that the reason spinners and pickers have more frequent anthrax infections is the more intimate contact that these particular workers have with the material. Particularly the spinners

at their machines are apt to get wounds on their hands while other workers might not be similarly exposed.

DR. MORTON: There have been reports that people have acquired anthrax by wearing a new jacket or airing new rugs. Do you think that wool sometimes gets incorporated into these garments, or articles such as rugs, without being dyed?

MR. PURDOM: Most of the material that goes into the interlining does receive a rather hot treatment before it leaves the plant. I would suspect that after that bath the material leaving the plant and going somewhere else to be incorporated in a suit jacket would not be apt to be infected. Probably the process would be of sufficiently high temperature for a sufficient length of time so as not to have viable organisms or spores present after that treatment.

DR. MORTON: Are there any other comments?

DR. WEDUM: I want to pursue this question of the spinners and pickers a little bit more. Is it a matter that the spinners and pickers are getting more finely divided dust on their hands or is it a matter of being more susceptible to minor abrasions on their hands and forearms?

MR. PURDOM: Particularly the spinners in their work might be apt to get a minor abrasion to the skin, and this intimate contact would provide easy means of infection.

DR. STEELE: I would like to ask of Dr. Schrack if he, in his search of the literature, has found reports of a second attack of anthrax in man.

DR. SCHRACK: I didn't find it.

DR. MORTON: Dr. Samuel Lodge, Jr., in the Archives de Medicine Experimentale et d'Anatomie Pathologique, II, 759-771, 1890,* reported

* References supplied during editing.

one patient who had suffered three attacks of pulmonary carbuncle in four years with recovery. I believe that the diagnosis was made on the basis of the clinical symptoms rather than on laboratory findings. Spear stated in his report (Tenth Annual Report of the Local Government Board, 1880 - 1881)* "On the so-called 'Woolsorters' Disease' as observed at Bradford and in neighbouring districts in the West Riding of Yorkshire" that from case histories which he had obtained it appeared that one attack of Woolsorters' disease successfully overcome confers no immunity for subsequent infection. One woolsorter had 5 distinct attacks in 17 years.

DR. BRACHMAN: In regards to the question of whether a second attack of anthrax occurs in an individual, I have come across a few references in doing some research reading on the subject. Philip Turner, in A System of Surgery by C. C. Choyce (1912),* reviewed the English cases of anthrax and mentions two patients who had previous malignant pustules. John B. Andrews, in United States Department of Labor, Bureau of Labor Statistics Bulletin No. 267, July, 1920,* mentions that two patients were reported to have had two attacks of anthrax. One patient had the second attack 9 months after the original attack. Dr. Herman Gold mentions in Tices Practice of Medicine (1952)* and Nelson's Loose Leaf Medicine (1946)* that there have been reports of patients who had two attacks of anthrax. Hodgson in the Lancet of June 28, 1941* reports two cases of recurrent cutaneous anthrax. One case was a veterinary surgeon whose two attacks were 3 years apart. In the other case the two infections were separated by an interval of only 6 weeks.

DR. MORTON: I wonder if that is truly a case of reinfection or could it be a case of reoccurrence of the original infection? It is known that an-

*Reference supplied during editing.

thrax bacilli, following an initial infection, may reside in the body for several months before the infection becomes active again. Was that point ruled out, Dr. Brachman?

DR. BRACHMAN: I think that point was questioned in one of the articles, but was not answered. It was brought up.

DR. MORTON: Perirenal abscess (Ercole and Fort, Anales de Cirugia, Rosario, 6, 263 - 284. 1940)* is not an unknown complication following malignant pustule and it may take place weeks or months after the initial pustule.

Mr. Purdom, you mentioned getting better lighting conditions in the working rooms, getting more daylight, in order to cut down the incidence of accidents. Might it be possible that by getting more daylight into a room, even though it is not direct sunlight, that there might be more rapid destruction of spores or organisms which are floating around? Are you considering getting more light from that angle?

MR. PURDOM: We mentioned lighting as a possible factor. I don't think we have enough data to indicate specifically what its influence might be. It had occurred to us that better lighting sometimes reduces industrial accidents and to that extent there might be less wounds of the skin and less occasion to have infection. What effect the light would have on the spores we have not made any tests to ascertain.

DR. MORTON: Have any of the plants installed ultraviolet lights in these rooms where there is a dust hazard?

MR. PURDOM: I don't know of any.

DR. VAN METER: I would like to ask Mr. Purdom whether or not

*Reference supplied during editing.

they have any data with respect to percentage of cases of industrial anthrax which are pulmonary anthrax. I get the impression from what has been said that the atmosphere of some of these plants is quite polluted.

MR. PURDOM: Practically all the cases are the cutaneous type that are reported to us, very few are the pulmonary type. I don't have the figures, but the number of pulmonary cases is very few. I think about two cases of the pulmonary type in recent history were reported; the rest of the cases are the cutaneous type.

DR. DAVIS: I would like to ask about the attack rate in these plants. They have given us the number of cases, but what risk is that to individuals on an annual basis?

MR. PURDOM: I don't have that data available at this time.

DR. MORTON: Are any studies underway to determine the extent of the exposure, that is, the number of spores that you might find in the atmosphere in some of these highly contaminated areas or the extent of contamination of the material that is shipped in and is handled?

MR. PURDOM: We have recently instituted some studies to determine that. We didn't have any data that we felt was worthy of presentation thus far, but we do plan to explore that further to determine the material that is in the atmosphere, its particle size, and whether or not it is contaminated with viable organisms.

DR. FOTER: I think this question was answered in Harrisburg, but I think I will bring it up because there are some people here who were not at the Harrisburg meeting. Are there any cases on record where anthrax has been disseminated, or carried over to farm animals, as a result of the workers in these areas, who might live in rural areas, taking it home to

to the farm of from the effluence of the plants that might be carried downstream and the cattle might become infected?

MR. PURDOM: As far as Philadelphia is concerned, we wouldn't have much likelihood of having a typical situation of the type to which Dr. Foter refers. If there are gentlemen from places that have mills in smaller areas they might be able to give an answer. Our situation would not be typical. We don't know of any cases that have occurred in that manner in this area.

DR. MUDD: I judge from the papers that all of the outbreaks in this country have been from imported sources. Is that correct? It has not actually become enzootic in American herds, is that correct?

DR. SCHRACK: I don't believe that is correct. Dr. Steele, perhaps you could tell us.

DR. STEELE: We have to go back into history to answer Dr. Mudd's question. There is no doubt that anthrax was originally introduced into this country by imported cattle in the southwest -- Mexico, Texas, and Louisiana -- and how it spread in the upper Missouri Valley and in California I wouldn't hazard any answer at this time.

The only record that we have of an anthrax outbreak being introduced in imported material was the bone meal episode that occurred in Ohio, Indiana, and Illinois two years ago.

Now to further answer this question that Dr. Foter posed before, there is one record in the United States at Greenville, South Carolina where there was an outbreak of anthrax on a dairy farm and the dairy did not take adequate precautions, in the opinion of the court when suit was brought, and the anthrax organisms were carried away in the effluent from the dairy that had the original outbreak and spread down along the water course.

MR. BUMFORD: In regard to one of the doctors' questions about workers in industrial plants carrying anthrax home, we have a number of them who maintain small farms and there has never been a case in New Hampshire to our knowledge of anthrax being transported from the humans to the animals.

MR. WILLARD: There is only one case that comes to my mind as far as Pennsylvania is concerned in that connection, I think it was back in 1940 that one of the plants in the Philadelphia area was accustomed to selling its dirt to a firm in New Jersey for fertilizer. At that particular time I believe a case of anthrax occurred in a farm area in South Jersey due to the use of this material as fertilizer.

My predecessor was on the case at the time, but I believe the records are in New Jersey. That is the only case we had of that nature.

DR. WITTE: I have made inquiry along similar lines in our own Department of Agriculture here in Pennsylvania. Of course, they have had anthrax in the past but they have never been able to trace it to a specific industrial origin, that is, as far as the worker transmitting the disease to the farm was concerned.

DR. MORTON: Mr. Purdom, I believe you made a statement that the shortest period in which a worker had contracted anthrax was something like two weeks; was it?

MR. PURDOM: Yes.

DR. MORTON: I believe in the literature there is on record that an individual worked just one day on a job handling hides and contracted anthrax, a case which I will mention this afternoon. It indicates that just a matter of a few hours' exposure was enough to contract anthrax infection.

MR. PURDOM: The point we were trying to make is that two weeks from the time of first employment is the period of time that we had a record of the person contracting the disease, not the length of exposure.

MR. STEIN: I would like to make a comment about tanneries and industrial concerns of that kind. A good many years ago, say, 30 or 40 years ago in Delaware, and perhaps 30 years ago in Virginia and about the same length of time in Connecticut, there were three different distinct outbreaks of anthrax traced to drainage from tanneries, and the reason for that perhaps was that there were pastures and farms very handy or in very close proximity to these industrial plants at that time.

Today in Delaware there are probably not nearly as many concerns handling hides, and the same way in Philadelphia and vicinity. Another thing: the land that was formerly occupied by farmers and used for pastures is no longer used for that purpose. At that time, though, it was definitely determined that these outbreaks were due to the drainage from the tanneries.

That point was made a number of years ago, but in recent years we have no evidence whatever that outbreaks in livestock have been due to these sources.

DR. WILBAR: Dr. Morton, since there has been a good deal of discussion about agricultural anthrax, it might be of interest to show what the statistics are in Pennsylvania. In the past 20 years there have been 21 cases, according to the Bureau of Animal Industry, of animals which have been reported as having anthrax and 7 of those were buffaloes from the Pittsburgh zoo.

DR. STEIN: I would like to ask Dr. Steele a question in regard to that outbreak in the Philippine Islands. I think you said there were about

25 cases. Is that right, Dr. Steele?

DR. STEELE: Yes.

DR. STEIN: And of those 25 cases that developed, there were very few cases, if I remember properly, that were due to intestinal anthrax. They were all of the cutaneous type. The curious thing about that is that where a number of natives will consume a carcass of an animal that has died of anthrax and will actually have handled the carcass and consumed parts of it, there will be a very small percentage who will contract intestinal anthrax. I think that is a point of great importance.

Another thing is that in civilized countries intestinal anthrax is very rare. In the United States I don't know of any cases that have been reported in recent years in the human, and I think the reason for that is that most of the meat that is consumed is subject to inspection, either by Federal or State authorities.

But this point that a lot of persons in the undeveloped countries will consume the meat of an animal that has died of anthrax and a very small percentage of them will actually contract intestinal anthrax indicates to me that perhaps there is an antagonistic effect on the anthrax organism when taken internally by either the human or animals.

I think it is almost necessary that there be an abrasion in the intestinal tract, some portion of intestinal tract, in order that either a bovine animal or any type of ruminant will contract anthrax; and the same is true of the human being.

DR. MORTON: I may not be absolutely right about this, but I believe that the intestinal tract is fairly resistant to infection by ingestion of spores, so it isn't surprising that animals and man do not very often contract the in-

testinal form of anthrax by eating infected food. It is true that the colon bacillus shows an antagonism for the anthrax bacillus. It might be that that is sufficient in the intestinal tract to prevent multiplication of the spores and invasion. Is there any other discussion?

DR. WILLARD: I have a question for Dr. Schrack, or in his absence, for Dr. Steele. I believe Dr. Schrack made a statement that the eighteen-year period up to 1951 shows Pennsylvania accounted for about 25% of the cases of industrial anthrax. I wonder if they have any figures on the relationship of the percentage of employee population in the anthrax industries in relationship to the total employed population in the United States, in the anthrax industries.

In other words, that would give us a better idea whether we are high, medium, or low.

DR. STEELE: I wouldn't be able to answer your question, but I think it could be calculated if you know the number of people who are working in these industries, which I suppose you could obtain from your Labor Department, and plot your cases against that and get a rate.

MR. DEVORRIS: On the statistics that Mr. Purdom gave concerning the cases of anthrax, does he differentiate between suspected cases and actual cases?

MR. PURDOM: The figures that I gave are those that were investigated by the Philadelphia Department of Public Health and indicated to be anthrax after that investigation.

DR. STEIN: I would like to make a comment about the transmission of anthrax by insects. In areas where agricultural anthrax is endemic, based largely on observation, the natives, many of the veterinarians and livestock sanitary officials believe that the disease is transmitted, after it once gets

started, by blood-sucking insects, such as the horse fly, stable fly, mosquito and so forth.

Incidentally, we have had during the last 20 years about 6 or 7 reports of anthrax in man following an insect bite, that is, the bite of a flea, bite of a mosquito or bite of a fly. Most of these cases occurred in an area where the disease was endemic.

A good many years ago there was a state veterinarian in one of the southern states who was out on a case and was accidently bitten by an insect, and three or four days later he developed a carbuncle. The idea was that he might have had anthrax on his hand and rubbed his hand over the area after he acquired the bite. That is a possibility.

Particularly in Louisiana long before any scientific evidence was ever presented to show that insects could transmit diseases, it was the opinion of the natives and many of the medical men there that anthrax outbreaks, that occurred way back in 1860 and even before that, always occurred when there was an abundance of insects. Oftentimes that natives would report the development of cutaneous anthrax following a bite.

There has been some scientific evidence backed up by very good research to indicate that certain types of insects will transmit the disease among animals, and that does not only include the blood-sucking insects. An insect that will fly on even a dead carcass and have its mouth parts, proboscis, and so forth, contaminated will fly onto a child with an open sore and deposit the organisms there and infect the child's face or arm, or onto an animal with an open abrasion. In other words, it is a purely mechanical transmission. There have been a number of reports indicating, for instance, in the Island of Haiti when an animal dies they will usually consume it unless it becomes so much decomposed that

they don't like to eat it on that account. They find out that many of these abrasions are caused by the bites of flies that have fed on the carcass that has been hung up to dry in the sun. In this way the fly will become contaminated with spores. When the contaminated fly then touches a child's face where there is already a sore, you will have an anthrax carbuncle contaminated with other types of organisms.

DR. FAGAN: I would like to corroborate some of the things that Dr. Stein said. I was told by an investigator that there was an outbreak in Rumania of anthrax, similar to the situation mentioned by Dr. Steele, where a bovine animal died and the villagers cut it up and ate it. The only type of anthrax that resulted was cutaneous anthrax, and for a certain reason, that reason being that the people carried the meat on their shoulders or else the lesions were around the part where they were bitten by insects.

In regard to Dr. Mudd's question about the way that these epidemics break out, Dr. Minett, of the International Office of Zoonotics, has studied the outbreaks, or has gathered all the statistics of outbreaks, occurring all over the United States or rather, all over the world. Incidentally, the United States doesn't participate in that. The vast majority of all agricultural anthrax arises from importation of contaminated food. Far and away there is no other single factor that comes close to it.

To set your mind at ease about Pennsylvania, the number of workers in the industries in Pennsylvania are at least 30% of the total leather, cartage, and so on. These will probably get lower as the industries move out.

DR. STEIN: I would like to make another comment about the fly problem. We captured flies in some of the severe outbreaks in South Dakota in 1937, when the last outbreak began. We brought them back to Washington, D. C., and were able to isolate very virulent anthrax organisms after they lay around for about

ten days or so in the laboratory.

These organisms were isolated both from the mouth parts and proboscis, and so forth, and from the inner parts of the fly. Dr. Stiles isolated the anthrax organism from ear ticks that he found on an ear, of an anthrax ear, that was sent into the laboratory for examination. These ticks are commonly found in the cattle ears, and without any difficulty he isolated anthrax from the ticks which commonly inhabit the ears of cattle. There is also the possibility that the disease might be transmitted by the variety of ticks.

DR. STEELE: The United States Public Health Service has recently prepared two film strips pertaining to anthrax. The titles of the film strips are "Epizootiology of Anthrax" and "Transmission of Anthrax - Animal to Man". The film strips and their accompanying transcriptions are available on a free loan basis from the Communicable Disease Center, Atlanta, Ga.

DR. MORTON: If there are no further comments we will adjourn for a short recess and reconvene in ten minutes.

Short recess

DR. MORTON: We will resume the presentation of papers. The first paper is "The Rapid Isolation and Identification of Anthrax Bacilli" by Dr. Kenneth L. Burdon, Professor of Microbiology at Baylor University College of Medicine, Houston, Texas. Dr. Burdon.

RAPID ISOLATION AND IDENTIFICATION OF ANTHRAX BACILLI

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It is some 75 years since the Bacillus anthracis was positively recognized as the specific causative agent of anthrax, and was the object of study by the most illustrious of the early leaders in bacteriology. Hence, it is indeed remarkable that we should still be concerned here and now with methods for carrying out the seemingly elementary task of isolating and identifying this bacterium. The explanation must lie principally in the fact that few bacteriologists have any real acquaintance with the group of aerobic sporeforming bacilli related to the anthrax organism, and classified with it in the genus Bacillus. There persists some confusion as to which of these related bacilli are most likely to be mistaken for B. anthracis and uncertainty as to the practicable means by which this possible source of error may best be circumvented. Only very recently has a greater degree of order been brought to our knowledge of variation within the species anthracis (3). When the grave responsibility of making a positive diagnosis of anthrax is unexpectedly faced by a diagnostic laboratory, it is no wonder that some uncertainty is felt as to just what needs to be done.

Often, current textbooks or manuals refer to Bacillus subtilis as the organism that must be distinguished from B. anthracis. This may be traced to a historical accident, which should have been understood and corrected years ago. When Dr. Novy came back to Michigan from his studies in Germany about 1890 he brought with him a culture of a large, chained, anthrax-like bacillus. Under th name of B. subtilis transplants of this culture were widely

distributed throughout the United States. But cultures of this so-called Michigan strain of B. subtilis now extant are indistinguishable from B. cereus. Since 1935 taxonomists here recognized as the true B. subtilis a small-celled species, quite unlike anthracis in morphology, and otherwise (13). It is B. cereus and not B. subtilis which must be differentiated from the anthrax bacillus. And here we run into real problems, for similarities are numberous and close, extending beyond in vitro reactions and behavior, since many strains of B. cereus appear to possess a definite, though low-grade, pathogenicity (1).

The practical bacteriological problems involved in the diagnosis of anthrax, and in the experimental study of the disease, are thus two-fold. First, what methods are to be recommended for the recognition of anthrax-like bacilli in the original material and for their isolation in pure culture, and second, how can a culture of B. anthracis be positively identified?

For a clinical diagnosis direct smears of the original specimen are helpful, though experienced workers agree that it would be hazardous to regard them as conclusive in themselves (9, 15, 16, 19). Gram-staining is of limited value, and may be misleading. These smears are best stained with polychrome methylene blue, or with toluidine blue. If a residue of capsular material is present, this will be revealed as an amorphous, purplish-colored deposit around the organisms - the so-called McFadyean reaction (11). Many times such direct smears from animal specimens, which have been some hours in reaching the laboratory, will show only a considerable number of rods suggestive of anthrax bacilli, but without any trace of capsular material.

It is imperative to culture the material as quickly as possible. We have observed that specimens kept for as long as 3 days may fail to yield a growth of the anthrax bacilli even though these were seen in the original smears. For the

primary cultures we suggest plates of two ordinary kinds of media, - plain tryptose agar (or trypticase soy agar), and a 7% sheep blood agar. It is well to inoculate three or four plates of each medium to reduce the chances of failure through the possible presence of rapidly growing spreaders, or organisms (e.g. Pseudomonas) which are strongly antagonistic to the growth of B. anthracis. The plates should be incubated at 37°C for 18 hours.

The relatively large, dull, anthrax-like colonies with their characteristic roughened (ground glass) surface, and wind-blown outline can be recognized without difficulty. On the blood agar the colonies of the true anthrax bacillus will invariably be non-hemolytic. For microscopic examination of likely colonies we now use the Gram stain, as well as polychrome methylene blue, and also the Sudan Black B fat stain (2). The organisms are now growing in the familiar long, parallel chains, and show the abundant large internal fat droplets characteristic of the anthracis-cereus-mycoides group. They are usually without any trace of visible capsule, and except for the fact they have formed a non-hemolytic colony, there is nothing which definitely indicates their identity as either anthracis or cereus.

The fastest way to settle the question is to prepare at once a saline suspension from several of these colonies (working preferably under a hood and with the aid of a wide-field dissecting microscope) and to inoculate each of 3 to 6 young white mice subcutaneously with 0.25 ml of this suspension. If virulent anthrax bacilli are present the mice will die in about 30 - 96 hours. When the necropsy is performed shortly after death there is a gelatinous local exudate, and direct smears from the spleen and heart's blood, stained with polychrome methylene blue, will always reveal numerous large rods, not in long chains, and now surrounded by an obvious capsule. Blood agar plate cultures

from the mice should result in recovery of characteristic rough, non-hemolytic colonies, containing the anthrax bacilli again in their long-chained, non-capsulated phase. If the mice should die in less than 24 hours, or only after 4 days or more, we should be suspicious, and if direct smears made shortly after death show only non-capsulated rods, even though these are numerous, we may safely conclude that the animal did not die primarily (at least) of anthrax infection, and the differential tests outlined below should be applied to the organisms isolated at the autopsy.

The mouse inoculations may, of course, be delayed until a pure young (12-18 hours) growth from a non-hemolytic anthrax-like colony on the original plate has been obtained. In that case we customarily prepare the inoculum by emulsifying a 3 mm loopful of the growth on a slant in 4.0 ml of sterile saline. From a portion of this a 1:2 dilution is prepared by adding an equal amont of saline. Each of 3-4 mice is then inoculated subcutaneously with 0.2 ml of each of these suspensions.

We have not given serious consideration to the use of any special selective medium for the primary cultures, such as the haemin-lysozyme medium of Pearce and Powell (12, 7). The latter, according to the author's own description, tends to suppress growth of anthrax bacilli as well as some other organisms, and does not help in differentiation of B. anthracis from B. cereus. We have tried the "sandwich plate" idea, used by Jones (10) and others (4), but think it of little positive value.

Since it has been shown by Chu (3) and by Thorne, et al. (18) that a characteristic of virulent, as distinguished from non-virulent, strains of anthrax bacilli is their requirement of increased CO_2 for formation of the capsule in vitro, a possible substitute for animal inoculation might be cultivation of a freshly isolated anthrax-like, but non-capsulated, strain on blood plates in an

atmosphere of 10 per cent CO_2 (3), or on blood media containing added bicarbonate (18). With our stock cultures this has worked very well; only strains of known virulence for mice produced visible capsules under these conditions. Not reliable, in our experience, is Ponder's modification of the McFadyean reaction by which a young growth of the unknown anthrax-like bacillus is incubated overnight in fresh human blood, then stained for capsules (10).

Turning now to the problem of demonstrating the presence of anthrax spores in feed, bone meal, soil, and similar materials, we find the task complicated by the multiplicity of bacterial species naturally present, and by the fact that growth of many of these bacteria is antagonistic to the development of anthrax bacilli. About 95 percent of these bacteria can be eliminated, however, by heating a suspension of the original material for only 5 minutes at 65°C (10). Antibiotics will not help, since B. anthracis itself is so susceptible (6). As a routine procedure we have mixed 11 grams of the feed or soil with 99 ml of buffered distilled water (pH 7.0), ground the mixture in a sterile mortar and filtered it through gauze. After the filtered suspension had stood for 30 minutes a portion was removed and heated as described. The heated material was (a) cultured on ordinary plain and blood agar media in a way similar to that described above for specimens from infected individuals, (b) cultured by a membrane filter technique, and (c) inoculated directly into mice.

For the membrane filter cultures a 1:1000 dilution of the heated suspension was prepared and three 100 ml portions were separately passed through isospore membranes. These cultures appeared to have some real advantages. They gave consistently higher total colony counts than agar pour plate cultures from the same inoculum. The membranes, colonies and all, could be saved, and filed for record purposes. Moreover, colonies of virulent B. anthracis

on the membranes would be distinguished from those of B. cereus; the former were delicate, transparent, and colorless, while cereus colonies were heavier, translucent, and yellowish. However, colonies of avirulent anthrax bacilli had intermediate properties. Despite the apparent advantages, we now feel doubtful that the membrane cultures are worth the extra effort involved. Antagonistic organisms, such as Pseudomonas, grow readily over the membranes and crowd out all the anthrax-like organisms. From contaminated soil, agar plates have yielded anthrax bacilli when the membrane cultures failed.

Most sensitive in detecting the presence of relatively few spores in such material as feed and soil has been found by us and by others (4) to be the direct mouse inoculation. Here we encounter, however, many deaths among the mice from toxicity of the original material, and especially from in vivo development of anthrax-like organisms having the properties of B. cereus. Thus, of 43 mice inoculated directly with heated suspensions from 12 separate bone meal samples originating in Ohio in 1952 and kindly sent to us by Dr. Bartram from the Food and Drug Administration, Washington, D. C., all but 7 died, - at least one mouse with each of the samples. These deaths occurred most frequently in less than 24 hours, occasionally after 4 days. Non-capsulated anthrax-like rods were seen in considerable numbers in spleen and heart blood smears in all but 3 of the dead mice. Traces of gelatinous exudate and a few capsulated bacilli, along with many non-capsulated ones, were found in two instances; B. anthracis could not be isolated. The three mice inoculated with bone meal specimen No. 805-5, all died in 36-48 hours. In only one of them was typical capsulated bacilli found in spleen smears, and a pure growth having the properties of B. anthracis was obtained from this single animal only. The ordinary cultures and the membrane cultures of the original heated material of the Ohio bone meal specimens

all failed to yield colonies of anthrax bacilli. We have had better results in this respect with soil materials obtained from the ground near the entrance to the post-mortem room at the A. and M. College in Texas. We dug up some soil a few feet away from the entrance, where the carcass was dragged over onto the floor of the room for postmortem, and we were able to isolate from two such specimens of soil anthrax bacilli. In this case they came out in the agar cultures as well as in the mice. The point that I wish to emphasize here is that from all of these cultures, whether you make membrance or agar plate cultures or inoculate mice, you will isolate a large number of anthrax-like organisms.

This brings us back to the differential tests which may be used to support the identification of a virulent capsule-forming bacillus as B. anthracis, and to recognize anthrax organisms whose virulence is reduced or lost. In general the differences between B. anthracis and B. cereus are chiefly a matter of degree, but a number of these differences are distinct and constant enough to be of practical value. The principal differential points are:

	B. anthracis	B. cereus
1. Hemolysis on sheep blood agar in 24 hrs.	none or slight	marked
2. Reduction of methylene blue in 24 hrs.	slight	advanced
3. Peptonization of milk	slight; delayed	marked; rapid
4. Fermentation of salicin	none	positive or negative
5. Growth on penicillin agar (10 units/ml.)	none or slight	good
6. Growth at 45°C (water bath)	slight or none	good
7. Motility	none	usually positive

It should be realized that no single one of these differential points should be counted on by itself to be definitive. There is no record of a motile anthrax bacillus or of one that ferments salicin. But non-motile cereus cultures have been known. Avirulent anthrax strains tend to approach in characteristics those exhibited by typical strains of B. cereus. Thus, the 25 mouse-virulent strains of B. anthracis in our stock collection all failed to grow on penicillin agar, but 12 out of 15 avirulent strains (each originally virulent and typical when isolated several years previously) were found to grow well, having lost their sensitivity to penicillin. A number of these latter strains also showed increased hemolytic and proteolytic activity. However, in no case did any single strain exhibit all the characteristics of a B. cereus. Similarly, the cereus-like bacilli so often isolated from various sources show some variation in the properties listed above, but no particular culture will have all the characteristics listed under B. anthracis.

The kind of findings one gets may be illustrated again by reference to the work with the Ohio bone meal samples mentioned above. Of 132 separate cultures of bacilli isolated from the original agar plate cultures, membrane cultures, or from mice at autopsy, all except one we concluded to be cereus-like, rather than anthracis. Of these 131 cereus-like cultures 125 (95%) were frankly hemolytic in 18-24 hours, while the remaining 6 had a sufficiently slight degree of hemolysis to suggest that they might be anthracis colonies. A total of 126 (96%) grew well on penicillin agar, while 5 did not grow, 91 (69%) grew at 45°C, and 69 (53%) fermented salicin. Only the single culture which was subsequently shown to be typically virulent for mice, gave essentially negative results in every one of the differential tests, as was expected of a virulent anthrax bacillus, that is, it was non-hemolytic, failed to grow on penicillin agar or at 45°C, reduced

methylene blue only slightly, did not change milk in 24-48 hours, did not ferment salicin, and was non-motile.

It appears that the highest degree of reliance in recognizing anthrax bacilli can be placed on their sensitivity to penicillin, inability to hemolyze blood actively or to ferment salicin, their lack of motility, and, of course, their capacity to form characteristic capsules, and to produce an overwhelming fatal infection from small inocula in mice or guinea pigs. It is our opinion that the ordinary "garden variety" of bacteriology we have described is adequate for studies of anthrax, provided one is aware of the necessity for thoroughness and care in all procedures.

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DR. MORTON: Thank you, Dr. Burdon. The next paper will be "The Efficacy and Application of Wool Sterilization in the Control of Occupational Anthrax," by Dr. James H. Steele, Chief, Veterinary Public Health, U.S. Public Health Service. Dr. Steele.

THE EFFICACY AND APPLICATION OF WOOL STERILIZATION IN THE CONTROL OF OCCUPATIONAL ANTHRAX

by
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Atlanta, Georgia

The sterilization of wool as a means of controlling occupational anthrax has been suggested for many years by health officials and interested persons. The first comprehensive report on the prevention of anthrax among industrial workers in England was by the Department Committee appointed by the British Home Office in 1915[1]. They presented their report in 1918, after a thorough investigation in which they came to the conclusion that precautionary measures were insufficient and that complete protection could only be afforded by disinfection of the raw material. They, therefore, made an extensive study as to the possibility of disinfection of wool without injury to the material. They succeeded in developing a procedure that has been in use for more than 30 years. The British Anthrax Prevention Act, 1919, (Appendix B) provided the Secretary of State with the necessary powers for the compulsory disinfection, on arrival in Great Britain, of any material likely to be infected with anthrax.

In 1921 a plant was established to process all wool and hair which was suspected of being contaminated with anthrax. This plant was erected at Liverpool adjoining the wool and hair warehouses. During the trial operations all East Indian goat hair and Egyptian wool and hair were disinfected. On arrival those products, as well as those to follow, were moved with the cooperation of the Board of Customs to the Government Wool Disinfecting Station. At the Station provisions were made for storing, disinfecting, and rebaling the hair and wool.

The process of disinfection is fully described in Volume I[1], but a sum-

mary is indicated here inasmuch as this presentation is a discussion of the efficacy and application of such procedures. The early investigations of the Committee revealed that disinfection of bales and fleeces was not always reliable except by methods which caused severe damage. It was also shown that anthrax spores in animal products of commerce are so well protected by nature (blood clots and fat) as to make disinfection very difficult unless the protection is removed.

The principle of disinfection as worked out by the British Committee is first to place the possibly infected material under conditions in which the natural protection is removed and the spores are exposed to the destructive effect of the disinfectants. The hair or wool then passes into the second stage in which the bacteria are destroyed.

The investigation showed that exposure to alkaline solutions at a temperature of 102° F (39° C) removes the protection of the spores and renders them susceptible to the action of disinfectants. The susceptibility increases, within limits, with the time exposed in this process. The minimum period recommended is 20 minutes. This exposure is followed by a 20-minute soaking in a solution of 2 1/2 percent formaldhyde, followed by drying in a current of hot air.

In 1949, when I had the opportunity to view the operations of the Government Wool Disinfecting Station in Liverpool, the same principles were still being used. The process consisted of seven consecutive steps:

(1) Exposure for 10 minutes, of the material to be disinfected, to the action of a solution containing 1/2 - percent of sodium carbonate at a temperature of 102° F.

(2) Exposure for 10 minutes in an alkaline solution of soap, containing approximately 1/4 - percent of soap, and maintained at a temperature of 102° F.

(3) Exposure for 10 minutes in a solution containing 2 - percent formaldehyde (CH_2O) and maintained at a temperature of 106° F.

(4) Exposure for 10 minutes in a solution containing 1.8 - percent formaldehyde (CH_2O) maintained at a temperature of 106° F.

(5) Washing or rinsing for 10 minutes in a constant flow of clean water, the formaldehyde content of which is maintained at less than 0.25 percent (CH_2O) and the temperature of the water at 102°.

(6) Drying and cooling preparatory to baling.

(7) Baling.

According to the Director of the Station, Mr. B. D. Nobs[2], the object of step (1) was to remove from the anthrax spores the albuminous protection which they always appear to have when present in wool and hair; of (2) was to bring the spores to a state in which they are easily destroyed; of (3) and (4) to cause destruction of the spores by the action of formaldehyde; and of (5) to remove the excess formaldehyde from the wool and hair.

Insofar as disinfection is concerned steps (1) and (2) are most important, and, unless these are properly carried out, disinfection by (3) and (4) becomes uncertain and difficult. The action of (1) is to dissolve away the protecting substances. The exact action of (2) is not clearly understood but anthrax spores are much more easily and certainly destroyed after this treatment. Step (5) is necessary because it was found that if formaldehyde is left in the wool, as was the practice in the early years of the application of disinfection, skin irritations associated with formaldehyde resulted amongst workers in the wool and hair industries.

The application of the process of disinfection is controlled in two ways (a) by routine chemical analysis of solutions and (b) by bacteriological examina-

tion of the materials before and after disinfection.

The strength of the solution at each stage is maintained by an apparatus which adds, at predetermined rates, a strong stock solution to the working solution, and these rates are adjusted in accordance with the results of the chemical analysis carried out on each solution every hour.

Bacteriological examinations of samples collected at the rate of approximately three per day before and after disinfection are carried out independently of the disinfection station. The time required for the complete passage of material through the machinery in the course of disinfection is approximately 1 hour and 20 minutes; therefore, a sample of the disinfected material issuing from the machine is taken 1 hour and 20 minutes after a sample of the raw material was taken as it passed into the machine. This is to insure, insofar as possible, that the samples of the disinfected material correspond with the samples of raw material.

The materials, in the course of disinfection, are passing through watery solutions for 50 minutes so that they are cleansed of most of the natural wool grease and foreign matters. Commercial wool and hair are bought and sold on the basis of containing 16 percent moisture and, insofar as possible, disinfected material is brought to this moisture content at the end of the disinfection process. To control this moisture, routine examinations of the finished material are carried out at intervals of approximately two hours, in addition to the practically continuous handling tests of the dried materials.

During World War II the plant was badly damaged and its operations almost stopped. A new addition was built in 1950 which is capable of handling 2,500 pounds of wool or hair per hour; the old plant handles 2,000 pounds per hour. About 7,000,000 pounds of wool or hair are disinfected annually, of which 90 percent is

goat hair. All animal hair imported through, or from, Egypt is treated. In addition to these treatments required by regulations, a fair amount of East Indian wool, bristles, horsehair, camel hair, human hair, and alpaca is voluntarily disinfected. Most of these products enter the United Kingdom through Liverpool, and those that come in through other ports are sent to the Liverpool Wool Disinfecting Station.

In 1950 the cost of handling these materials was 2 pence per pound (raw weight) for hair and wool, and 3 pence per pound for bristles. This cost covered renewals and repairs to machinery, rents, maintenance and operating costs. The capital cost of the new addition was estimated at $300,000.

At one time the British Government planned to turn the station over to the League of Nations', Health Division, to be operated as an international station under the League's supervision. It was also planned that the League of Nations would establish other stations throughout the world. Some authorities are of the opinion that the World Health Organization should consider this plan inasmuch as disinfecting stations in countries of origin would prevent the exportation of contaminated fleeces, hair, and bristles.

Before discussing the results of this program, it is well to point out that more than one-third of the samples which are examined at the University of Liverpool School of Tropical Medicine Laboratory and at the Bradford Public Health Laboratories yield Bacillus anthracis. These samples are taken from the bales as they are opened for disinfection. All kinds of wool and hair are found contaminated but most isolations are from the products of Southern Asia.

The results of the program have been considered worthwhile by British public health and labor authorities. About 30 cases of industrial anthrax have been reported annually in Great Britain since World War II. Only about 20

percent of these cases occurred in the wool and hair processing industry, whereas in hide industry had 80 percent. No reported cases were attributed to goat hair. Prior to the disinfection program more cases were caused by goat hair than by all other sources together. The Wool Disinfecting Station has had a few cases nearly every year since opening in 1921. In 1948, 5 cases were reported. They were all successful treated with penicillin. Previous to the availability of penicillin, hyperimmune serum was used.

The question has been raised in recent years of why could not a similar system be established in the United States. The first consideration is: What is the size of the problem in the United States? Figure 1 depicts the incidence of reported human anthrax for 1944 - 1953. The annual average for that period is between 50 and 60 cases.

Wolff and Heimann[3] have pointed out that 82 percent of the industrial anthrax cases occurred among workers in those industries processing animal hair and wool during the 1939 - 49 decade. In this same period the average number of cases reported annually from the hair and wool industries was over three times the annual average for the preceding 20 years. Data were collected on 530 industrial anthrax cases due to animal fiber, for the years 1934 - 1949 inclusive. The breakdown of these 530 cases is as follows: hair, 116; wool, 366; hair and wool, 48. Thus, of the 482 cases due to either hair or wool, 24 percent were attributed to hair and 76 percent to wool.

The data collected for the 82 cases caused by animal hair were divided as follows: 74 cases charged to goat hair; 5 to horse hair; and one each to cow hair, camel hair, and bristles. Information was obtained on 66 of these cases which revealed that the countries of origin as as follows: India and Pakistan, 59; China, 4; South American countries, 3. All of the 59 cases charged to India

or Pakistan were due to goat hair. Two of those charged to China were also due to goat hair. These data reveal that over 90 percent of the hair cases were attributed to goat hair and that 95 percent of them originated in India or Pakistan. It is interesting to observe that of the 203 cases due to hides, on which data were obtained, goat hides and skins from India or Pakistan were the source of most of the cases that could be traced to country of origin.

The average imports of hair in the United States, according to government figures for 1939 - 1949, are shown in Table I. This table shows for 1949 that the United States imported goat hair in an amount two and one-half times as great as the total British importation of wool and hair; the processing cost of the British importation was $165,000 which did not include capital investment for buildings and machinery.

Wolff and Heimann[3] in their excellent report point out that 76 percent of the industrial anthrax cases attributed to animal fiber were reportedly due to wool alone. Unfortunately, they were not able to obtain data regarding the countries of origin. Of the 365 cases on which information was obtained, carpet wools (usually the coarser grades of fiber) were responsible for 315; the origin of the other 50 cases was unknown. No cases were attributed to apparel wool. It thus appears that industrial anthrax ascribed to imported wool is uniquely a carpet wool problem, even though the consumption of foreign wool by the apparel wool industry exceeded by more than twofold that of the carpet industry.

Table II lists the geographical areas of the world from which the United States imports wool and the amounts of fine and coarse wool imported. This table indicates which areas are least likely to be the source of anthrax-contaminated wools; that is, those countries which export fine wool for the apparel industry. Conversely, the areas exporting coarse wool are usually thought of as

having a high incidence of anthrax with the exception of Argentina, Great Britain, Ireland, and the Union of South Africa, which countries have well organized livestock disease control programs. The areas which have a high incidence of animal anthrax are Southern Europe, North Africa, Western and Southern Asia, and China. The average wool imports from these areas during the 1940 - 1949 decade were 44 million pounds annually. The carpet industry consumed 43 million pounds while less than one million pounds were used by the apparel manufacturers. These imports from anthrax enzootic areas constitute 6.1 percent of the total wool imports of 712 million pounds. This 44 million pounds of possibly contaminated wool, plus the 17 million pounds of hair, constitutes the principal source of industrial anthrax ascribed to animal fibers.

Wolff and Heimann[3] have further classified the animal fibers into four categories depending upon the degree of anthrax risk attached; namely, (1) very dangerous; (2) dangerous; (3) not without risk; and (4) without risk. The "very dangerous" according to their classification would include all non-grease wools, except washed fleeces, imported from Asia, Africa (except the Union of South Africa), and Southern Europe. The "very dangerous" category would also include all goat hair from Asia. The "dangerous" materials would include all other animal materials from Asia and Africa (except the Union of South Africa). "Not without risk" would include all animal material from South America except wool, and all other materials from Southern Europe. "Without risk" would comprise all fine wool and animal materials from Canada, Great Britain, Ireland, Union of South Africa, New Zealand and Australia.

To eliminate all possible exposure to anthrax-contaminated animal materials would require the prohibition of entry of all classes of animal material

except those "without risk". Obviously, this could not be done for it would disrupt commerce and industry. In the past there have been many advocates for compulsory disinfection of potentially infected imports. Hides and skins can be dismissed from this discussion inasmuch as there is no known economically satisfactory method of disinfecting them. However, the British method used for hair and wool has been proven an effective disinfecting procedure in Great Britain. If this process were applied to all dangerous hair and wool imported into the United States it would require the disinfection of more than 60 million pounds of animal fiber to insure reasonable protection. Wolff and Heimann in 1949 estimated that the inauguration of such a procedure in the United States would necessitate the initial investment of several million dollars and would probably raise the costs of the processed materials 5 to 10 cents a pound. It would be necessary also to centralize a disinfecting station in the United States so as to reduce the hazards involved, and for economical administration. This would result in the loss of commerce to the ports that did not have the disinfecting station. Hence, there are many reasons why the British disinfecting system would not be practical in this country even though it is recognized as being an effective means of destroying B. anthracis.

The incidence of industrial anthrax can be held to a minimum by the adoption of the following procedures which were developed by Wolff and Heimann and later adopted by the World Health Organization.[4]

1. All dusty operations in leather and wool textile industries, wherein potentially infective materials are handled, should have adequate exhaust facilities and should be isolated from other operations.

2. Floors, walls, stairways, elevators, etc., should be of such construction that they may be readily cleaned by wet sweepting or vacuum cleaning;

cleaning should be done daily.

3. All dust, dirt and sweepings should be incinerated.

4. Blending, whenever compatible with the manufacturing process, should be conducted after scouring

5. Scouring should be as efficient as possible; the circulation of clean water while draining off the sludge would increase the efficiency.

6. Drying of wool should be conducted at the maximum temperature compatible with the process.

7. Rawstock dyeing in preference to skein dyeing should be used as much as possible.

8. No wools except those classified as "without risk" should be allowed into the final product without having been dyed.

9. Finished products and dyed wool and yarn should be handled and stored in such a manner that there is no danger of cross contamination from dust, dirt, grease, and excrement from raw materials.

10. If, as is suggested under control methods for "import materials", bales of raw materials are tagged according to degree of anthrax risk, these tags should be left on the bales until such time as they are opened and their contents removed.

In addition, it is necessary to develop a good medical and health education program for the plant employees. This should include:

1. Facilities available for early diagnosis and treatment.

2. Indoctrination of employees with the necessity of reporting cuts, scratches, abrasions and pimples immediately. Medical or first aid attention should be given such lesions.

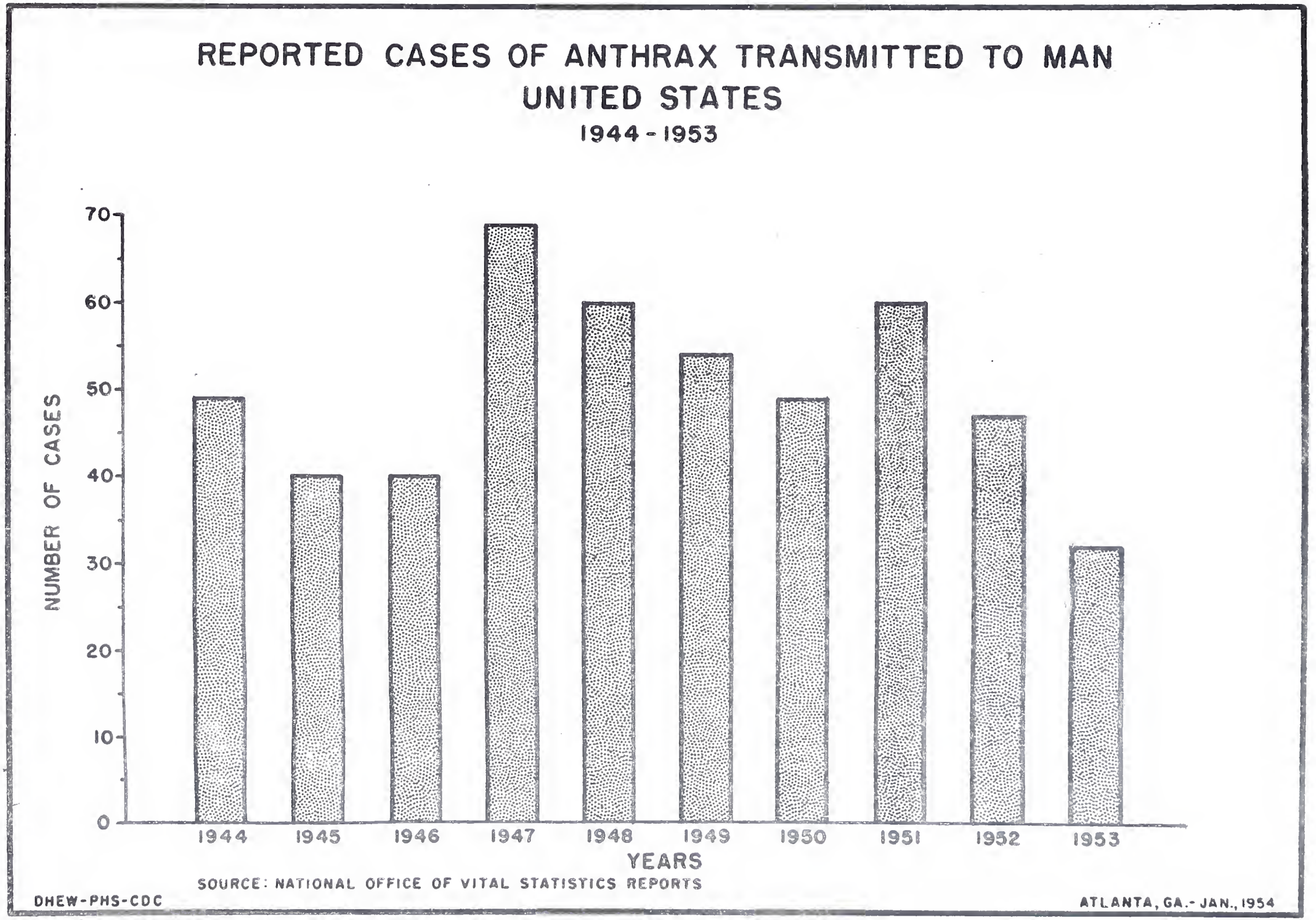
3. All employees properly indoctrinated on the cause, nature and con-

trol of anthrax. Posters and pamphlets, in appropriate foreign languages, if necessary, should be freely used.

Before closing, I would like to mention briefly the impact of advances in medical therapy on anthrax. The rapid development and proven effectiveness of antibiotics in the past decade have modified the concern of health authorities in regard to human anthrax. Prior to 1945, mortality from anthrax was high but with the advent of the antibiotics the mortality rate has dropped precipitously. This is also true of animal mortality. During recent years the veterinary medical literature has carried numberous reports on successful therapy of anthrax infections in cattle, swine, and mules.

The control of anthrax in the United States requires constant surveillance in addition to a hygienic, medical, and educational program. A surveillance program has been established by the Communicable Disease Center which will attempt to collect epidemiological data on all human cases of anthrax in the United States. This program should eventually contribute to a broader knowledge of the epidemiology and control of anthrax.

Figure I


REPORTED CASES OF ANTHRAX TRANSMITTED TO MAN
UNITED STATES
1944 - 1953
NUMBER OF CASES
70
60
50
40
30
20
10
0
1944
1945
1946
1947
1948
1949
1950
1951
1952
1953
YEARS
SOURCE: NATIONAL OFFICE OF VITAL STATISTICS REPORTS
DHEW-PHS-CDC
ATLANTA, GA.- JAN., 1954
54-1327
DHEW-ATLANTA,GA.

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APPENDIX B

ANTHRAX PREVENTION ACT, 1919

AN ACT to control the importation of goods infected or likely to be infected with Anthrax, and provide for the disinfection of any such goods. (22nd July, 1919)

Be it enacted by the King's most Excellent Majesty, by and with the advice and consent of the Lords Spiritual and Temporal, and Commons, in this present Parliament assembled, and by the authority of the same, as follows:-

1. (1) His Majesty may by Order in Council make provision for preventing the importation into the United Kingdom, either absolutely or except at any specified conditions as to disinfection and otherwise, of goods infected, or likely to be infected, with anthrax (in this Act referred to as "infected goods").

(2) An Order under this section may contain a declaration that goods of any specified class which are of any specified origin, or are exported from or through any specified country or place, are goods likely to be infected with anthrax, and any such declaration shall be conclusive for all purposes.

(3) Any Order made under this section may be revoked or varied by any subsequent Order.

(4) An Order in Council under this Act may apply, as respects any goods specified in the Order, any of the provisions (including penal provisions) of the Customs (Consolidation) Act, 1876, or any Act amending or extending that Act, with respect to goods whereof the importation is prohibited under those Acts, with such modifications as appear necessary or expedient, and in particular with the substitution of Secretary of State for the Commissioners of Customs and Excise, and of persons appointed by the Secretary of State for officers of Customs and Excise.

(5) In this section the expression "specified" means specified in an Order made under this section.

2. (1) A Secretary of State may provide, maintain, and carry on, or arrange for the provision, maintenance, or carrying on, at such ports or other places in the United Kingdom, as he thinks proper, the necessary works for the disinfection of infected goods, and may make rules providing for the payment by importers of infected goods of fees in respect of the disinfectant thereof, and in respect of services rendered in connection with such disinfection, and for the recovery of such payments.

(2) Any expenses incurred by the Secretary of State in carrying this Act into effect, up to such an amount as the Treasury may approve, shall be defrayed out of the moneys provided by Parliament.

3. This Act may be cited as the Anthrax Prevention Act, 1919.

TABLE I

Average annual amount of goat hair in millions of pounds imported to the United States for consumption according to geographic origin, by 5-year periods, 1939-1949, inclusive

YEAR	Total animal hair*	Goat hair			
		TOTAL	Geographic origin		
			India and Pakistan	China	/Others
1939-43	13.9	6.4	3.9	.3	2.2
1944-48	18.0	9.0	5.1	.7	3.2
1949	17.0	9.3	5.8	1.1	2.4

*Hair of bovine and equine origin constitutes most of the imports which were not caprine

/Principal countries other than India, Pakistan and China exporting goat hair to the United States are Turkey, Russia, Iran, Iraq and Latin American countries.

Source: Reference No. 3

TABLE II

Average annual amount of fine and coarse wools imported to the United States for consumption according to geographic origin: 10 years, 1940-1949 inclusive

Geographic Origin*	Average annual amount in millions of pounds		
	Total wools	Grade/	
		Fine	Coarse
All countries	712.0	517.0	195.0
Australia and New Zealand	290.0	282.0	8.0
Argentina	216.0	86.0	130.0
Africa	50.0	48.0	2.0
India and Pakistan	19.2	0	19.2
Western Asia	15.2	0	15.2
British Isles and Eire	10.0	1.0	9.0
China	6.9	0	6.9
Southern Europe	2.1	0.1	2.0
Other Countries	103.0	100.0	3.0

*Western Asia includes Aden, Afghanistan, Arabia Peninsula States, Iran, Iraq, Saudi Arabia, Syria, Transjordan and Turkey.

Southern Europe includes Greece, Italy, Portugal, Rumania, Spain, Yugoslavia and the Islands of Cyprus, Malta and Gozo.

China includes China proper, Manchuria, Mongolia and Tibet.

Africa includes all African countries. However, fine and apparel wools originate primarily in the Union of South Africa. The coarse wools originate primarily in the Northern part of Africa, including Algeria, British East Africa, British Somaliland, Egypt, Ethiopia, Italian East Africa, Morocco, Libya and Sudan, with Egypt being the principal source of coarse wool.

"Other countries" are predominantly Latin American Countries other than Argentina.

/"Fine" includes all wools finer than 40's and "coarse" includes all wools not finer than 40's.

Source: Reference 3

Reference

1. Home Office, Departmental Committee, Disinfection of Wool in Great Britain, His Majesty's Stationery Office, 1921.

   Vol. I - Report of the Disinfection Subcommittee, 1918
   Vol. II - Report of the Committee, 1918
   Vol. III - Summary of Evidence and Appendices, 1918

2. Nobs, B. D., Director, Government Wool Disinfecting Station, Liverpool, England, Personal Communication, 1949.

3. Wolff, Arthur H. and Heimann, Harry. Industrial Anthrax in the United States. Amer. J. of Hyg. Vol. 43, No. 1, Jan. 1951.

4. World Health Organization Technical Report Series No. 40: Joint WHO, FAO Expert Group on Zoonoses, Report on the First Session, May, 1951.

DR. MORTON: Thank you Dr. Steele. The next and concluding paper for this morning's session is entitled "Industrial Methods and Plant Design as Related to Employee's Health". It will be presented by Mr. C. D. Yaffe, Senior Sanitary Engineer and Chief, Engineering Services of the Occupational Health Field Headquarters, United States Public Health Service, Cincinnati, Ohio, Mr. Yaffe.

INDUSTRIAL METHODS AND PLANT DESIGN AS RELATED TO EMPLOYEE'S HEALTH

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U. S. Public Health Service
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When we undertake to do something, we usually assume a degree of risk. A task as simple as hanging a picture may result in a mashed thumb. When we take on multiple operations such as is ordinarily the case in industry, we find ourselves faced with a multiplicity of hazards; but the presence of danger seldom stops people from trying to achieve their ambitions.

A significant development, particularly of the Twentieth Century, however, has been the movement to protect the individual against the hazards of life. This movement manifests itself through many channels such as public health agencies, insurance companies, educational institutions, safety organizations, and volunteer groups. As a result, we now have traffic lights and safety goggles, fire departments and physical examinations, exhaust ventilation and vaccinations; and though too many still die on our highways, and from disease, and from poisonous fumes, we are making progress. The techniques for prevention have, in most cases, been worked out and perfected. The remaining job is to make the maximum practical use of the knowledge gained. In many cases this involves taking methods used in one situation and adapting them successfully to another.

The subject of this Symposium is "Anthrax in Man". Many of the cases of anthrax seen in humans nowadays result from occupational exposures. My task today, as I see it, is to review the principles employed in the control of other industrial health hazards and to see which ones might be employed in ef-

forts to reduce the incidence in industrial anthrax.

The control of airborne contaminants in industry is accomplished in many ways. All of them, however, fall into one or more of the following categories:

1. Substitution of material
2. Change of process
3. Enclosure
4. Isolation
5. Dilution
6. Local exhaust ventilation
7. Housekeeping
8. Personal protective equipment
9. Education

Substitution, where possible, is an ideal method for the elimination or reduction of a health hazard in industry. An outstanding example of the application of this principle was the substitution of comparatively non-toxic Glauber's Salt for the mercury nitrate which was the cause of widespread mercury poisoning in the manufacture of felt hats. Many other examples of substitution, particularly in the use of solvents, can be found.

Let us consider the substitution principle with respect to anthrax. The original source of the anthrax is contaminated raw material. Obviously, if we stop using contaminated raw material, we can eliminate the problem. Where or how do we get non-contaminated material? Sterilization of raw materials, if effective, provides one method, assuming that sterilization is economically practical and that the sterilization process does not have an injurious effect on the material. Sterilization cost may be relatively unimportant in one instance but entirely too great in another. Another way to eliminate contaminated material is to go to anthrax-free sources, if such sources of suitable material are available. I say "if" because it is my understanding, for example, that wools from some localities that are reportedly free of anthrax may be suitable, let

us say, for clothing not for carpets. Another way to eliminate the anthrax is, of course, to substitute a material where the organism should be absent, such as synthetic fibers like rayon and nylon. It is evident that quite a shift to synthetic materials is taking place in the textile field; and while it is unlikely in many cases that anthrax was even thought of in reaching the decision to change to synthetic fibers, this trend will undoubtedly effect some reduction in the incidence of anthrax.

It is evident, therefore, that the principle of substitution should be considered in approaching the problem of anthrax control.

Industrial health hazards sometimes can be eliminated or reduced by a change of process. The noise problem arising from riveting can be eliminated by a switch to welding. Conversely, the hazard from welding fumes can be eliminated by a switch to riveting. This example is given to show that in striving to correct one problem we must be careful not to create another.

One change which is frequently employed involves the use of wet processes. Wet drilling for dust control is a good example. Studies made several years ago by the late Dr. Roy Schneiter of our Division showed that in plants using contaminated wools very few anthrax spores could be found in the departments handling scoured wools, while comparatively many spores were located in those operations preceeding scouring. It is most likely that airborne transmission of dust from contaminated areas accounts for the few organisms found in areas handling only scoured materials. This suggests, therefore, that consideration be given to procedures whereby scouring can be done as soon as possible. Dust control is undoubtedly important in preventing airborne anthrax in industry, and wetting the material is an excellent way to stop the dispersal of dust.

Enclosure of dust sources such as transfer points on conveyors handling crushed stone is a simple, practical, and widely-used control measure in industry. It is a principle which might well be employed more extensively in some plants handling contaminated materials.

The principle of isolation involves locating a hazardous process away from workers. This usually means a different physical location, but sometimes means an isolation by time. For example, in many mining operations the blasting is done at the end of the work day after the men have left; and time is provided for the blasting gases and dust to be dissipated before anyone re-enters the mine. Time isolation might have some value in anthrax control, but it would probably be very limited because of the prolonged viability of the spores. Physical isolation of contaminated material would seem to be of much more practical value. The physical separation of departments handling scoured wools from those handling raw wools would certainly confine the problem to a smaller area.

Dilution, which is synonymous for general ventilation, has wide industrial application for protecting workers against the effects of dusts, gases, fumes, vapors, and mists. If sufficient clean air is introduced, concentrations of toxic contaminants can be reduced below the minimum levels capable of producing significant injury. I am uncertain, however, as to whether any number of anthrax spores above zero can be considered as permissible. Lacking a reliable limit, I would not wish to rely on the dilution principle in this case. Furthermore, consideration should be given as to the fate or destination of spores removed by dilution. This principle involves the use of such large volumes of air that it is generally impractical to subject it to any cleaning process. Organisms removed by this method, therefore, are free to travel where the four winds may take them. I am not prepared to state how serious a problem this may be.

At least it must not be overlooked.

If ventilation is to be used for anthrax control, the principle of local exhaust seems to offer much more promise. Local exhaust ventilation is one of the most useful tools of the industrial hygiene engineer. It involves removing the contaminant as near as possible to its point of release, the idea being to keep the offending agent from ever getting a chance to disseminate into the general atmosphere. This is accomplished by suction which pulls the contaminant through a hood into an exhaust duct. The volume of air used is far smaller than is required for dilution; and it is more practicable to discharge the contaminated air through a suitable cleaning process, thereby preventing an air pollution problem.

The use of properly designed local exhaust ventilation can provide very material assistance in preventing the dissemination of anthrax spores throughout a plant. It is particularly important as a control measure at the point where bales of raw material are first opened.

The value of housekeeping in the control of industrial health hazards is frequently underestimated, particularly where exposures to toxic dusts are involved. With respect to the anthrax problem, good housekeeping is definitely essential; and all suitable housekeeping methods should be employed. This would include not only cleaning methods conducted so that dust is not stirred up in the process, but other measures which will prevent the spores from moving about. Frequent painting of walls, for example, ties down spores on such surfaces, eliminating them as potential sources of disease. Fresh paint also encourages overall cleanliness.

I would like to mention at this point that Mr. Purdom's remark about the absence of the disease where there was good lighting interested me very much. I think the same idea that is expressed here is pointed out there. Good

lighting, if nothing else, encourages good housekeeping. It might be that there is a lower incidence of the disease because of the fact that they are keeping the plant cleaner.

Fumigation of part or all of a plant probably could be classified as a housekeeping measure, but I doubt the value or practicality of such a procedure unless it is to be immediately accompanied by other measures which will prevent recontamination.

Personal protective equipment is frequently recommended in industry but should be considered as a supplemental control measure and not a substitute for environmental controls. With respect to anthrax, I should like to quote the following recommendations by Wolff and Heimann[1] from their report on "Industrial Anthrax in the United States".

"Personnel protection. 1. Protective clothing should be worn by employees in all occupations where an anthrax risk exists. Such clothing and arrangement for laundering should be encouraged by management. The clothing should consist of loose fitting coveralls with long sleeves and collars, and hats. Boots and aprons impervious to water should be available for workers in wet processes. Wearing of gloves should be mandatory in all instances in which it would be compatible with the process. The wearing of respirators may be necessary at certain dusty operations.

"2. Adequate lavatory and locker space should be made available. Two lockers should be available for each worker exposed to risk: one locker for street clothes and the other for work clothes. Workers exposed to risk should be required to take showers and change completely from work clothing to street clothing before leaving the factory."

Before taking up the last of the items originally listed, I would like to

say something about plant methods and design.

It is common practice in plants processing wool and other fibers to move material from one operation or location to another by blowing it through ducts. Since these are under pressure, they represent sources of dust at all points where there is any leak. In addition, they are naturally dust sources at discharge points. Consequently, if infected material is moved through such a system, spores are bound to be discharged into the air.

I have seen one plant where material is moved through ducts by vacuum rather than by pressure. In this case, if there is any leakage in the system, it is into the ducts, not out of them. The material moving system is thus eliminated as a major mechanism for the spread of contamination.

There is not much difference between a system operated under positive pressure and one operated under negative pressure; and theoretically, a conversion could be made merely by relocating the fan or blower. Actually, of course, conversion of an existing system in a plant might present many practical problems; and the cost might be exorbitant. The possibility of conversion, however, is at least worth considering where anthrax is a problem. Where a new plant is to be built, the value of a negative pressure system should definitely be weighed since it offers many advantages such as reduced housekeeping costs.

If the plant designers are aware of the problem, they can design structures, equipment, and methods which will materially reduce the difficulties of coping with anthrax. It is this "if" which brings us back to "Education", the final category I had listed. The control of any industrial health hazard is possible by proper application of the control principles which have been outlined, provided that both workers and management know why control is needed and how it is to be effected. The more difficult the problem, the greater the need

for education. In the case of anthrax, both environmental and personal control measures must be employed; and the reasons for both types must be understood if they are to be properly used and completely effective.

This Symposium certainly represents a big step forward in the educational process.

1. Wolff, Arthur H. and Heimann, Harry: Industrial Anthrax in the United States - An Epidemiologic Study. Am. J. Hygiene, Vol. 53, No. 1 80-109, Jan. 1951

DR. MORTON: Thank you, Mr. Yaffee. The last three papers are now open for discussion. Does anybody have questions which they would like to ask the speakers?

MR. WIELAND: Dr. Steele, I believe you stated in your paper that in 1942 to 1950 the sterilization station at Liverpool was out of commission for a period of time in certain respects. Do you have any statistics on any increase in anthrax during that period of time?

DR. STEELE: The statistics that were available were related to me verbally. They pointed out that during that period of time they were not importing fine cashmere fleeces, goat hair or bristles that would ordinarily be coming from the grossly contaminated areas. Most of the woolen goods that they were using during the wartime periods were actually being processed in this country and being shipped to England as finished material.

DR. FOTER: I would like to ask Dr. Burdon (he may have brought this out in his paper and I may have missed it): when the membrane filter is used for the cultivation of the organisms from the material that you are testing, do you use a special nutrient medium that you put on the pad or is it the same medium that you use in the agar plates minus the agar?

DR. BURDON: We used an enriching broth.

MR. WILLARD: Dr. Steele, another question. In your talk you reported, referring to Wolff and his associates, and their article that in relation to the vital statistics the cases reported are not a true picture of what might have occurred.

I will put you on the spot here, I realize, but in your opinion do you think that the extra ordinarily high rate of anthrax in Pennsylvania might in a measure be due to the strictness and the veracity of reporting in Pennsylvania?

DR. STEELE: I would think so.

There is a gentleman here from New Hampshire and he may be able to relate the circumstances that came up in connection with my paper which was published two years ago. In that paper we did not have the New Hampshire statistics reported to the National Office of Vital Statistics, and immediately after the paper appeared he called to our attention that they had not been reported in New Hampshire within recent years, although they had been collected within the state. Those things are constantly occuring in many diseases.

A beautiful example that always comes to my mind is glanders. Dr. Fagan remembers our experience in Indiana some years ago when I asked Dr. Fagan to check on a case and he said the girl in the office in the local health agency didn't know what glanders was, and it was just a matter that it got in the wrong column. The same thing can occur again. They had 16 cases reported for the State of Iowa this year and I know when the inquiry comes back they'll say it's a typographical error.

DR. WERRIN: I am under the impression that the cases of anthrax that are being reported in Philadelphia do not represent the entire picture. I believe there are many more cases that occur in this city that are not reported, actually. I always come across some physician who says, "Oh, yes, I have

seen a case of anthrax two or three weeks ago". When I ask, "Did you report it?" the answer may be, "Oh, no, I didn't report it".

Of course, I am not too sure that it might not have been some other condition, but he actually used the word anthrax and that is when my ears always perk up. But I am pretty sure there might be some more cases that are unreported. It might be for a definite economic reason that they are not reported -- insurance, and so forth.

DR. BONDI: Dr. Burdon in his discussion of methods of separating B. cereus from B. anthracis failed to mention anything about the possible use of a true patient test. Do I infer from this that the two organisms are so closely related antigenically that you couldn't conceivably separate them?

DR. BURDON: I have no experience that has any weight, really, on that. We did make a test some years ago. We thought it wasn't any good, but I am not prepared to say that it cannot be done. I would like to turn the question around: Do you have any experience?

DR. BONDI: No, I am actually more interested in it from a theoretical point of view than a technical point of view, although I see no reason why it might not be a valuable tool if the two organisms aren't sufficiently different.

DR. BURDON: They are extraordinarily alike and unless one has some special method you can't get an emulsion, I know that. You can't do it very well.

DR. MORTON: I would like to ask Dr. Bondi if he has any remarks to make concerning the sterilization of wool or hair.

DR. BONDI: I have had no experience at all regarding the sterilization of wool and really have nothing to say.

MR. PURDOM: In Philadelphia there is one plant that is shifting a considerable amount of material called tops to a plant in another location and

it is my understanding that they have a small steam sterilization chamber and tests run by a private laboratory show favorable results on the use of that material at a relatively low cost.

We haven't made enough studies of this at the present time to report any data on it. I wonder if Dr. Steele would want to comment on the practicality of perhaps a plant having a small sterilization operation by itself as contrasted with this large sterilization unit that would handle, say, all of the material of all the plants. Is there any indication that a small unit in an individual plant might be practical as contrasted with the larger unit?

DR. STEELE: I'll refer the question to Mr. Yaffee who has had experience with industrial layout and plant design and management. I think the final analysis there is comparing the problem with the cost, and the situation you are referring to there -- that the state where that material is being shipped to set up regulations requiring that all material of that type which comes into that state had to be sterilized from that day on because they did not want to have any further experience of that type.

I think it would be well to just mention briefly what that experience was. A plant in one of the southern states was using this material and had been using it for some time. They had used an old building and readapted it to their procedures, while they were considering building a new one. One case of cutaneous anthrax occurred in a woman working in this plant. The State Public Health officials became very much concerned as well as the Animal Health officials because they had previously had the experience where a dairy had contaminated effluents going downstream and farms had outbreaks of anthrax.

They were very much concerned about what this was going to mean from a public health and animal health point of view. In addition, some studies made

at the plant indicated that you could isolate anthrax spores in any dust that was collected on the machinery, window ledges, locker rooms, the manager's desk or just by air sampling. So the State wanted to take precautions and in that instance I felt they were justified.

But to lay down an overall rule, I think you have to have good industrial engineers evaluating your problem to determine what the costs were. I am firmly of the conviction that where you have good plant management, where they can separate their operations and have a certain group of people who have been doing one operation under constant surveillance and have a good medical care program, that the problem can be handled in that manner.

MR. VAN NESS: I have a question of Dr. Burdon. He started speaking of the isolation of B. anthracis in bone meal and soil and then he gave the instance in which he isolated the anthrax organism near a place where anthrax had been diagnosed.

I have gone over the literature available on anthrax and I would like to ask Dr. Burdon if he has ever isolated anthrax organisms from a farm on which anthrax occurred, but from a region removed from where an animal died. That is, most of the anthrax that we encounter occurs in these anthrax districts, but attempts to isolate the anthrax organism from the farm have up to now, as far as I can find, been futile.

Will Dr. Burdon tell us if he has isolated it from Texas soil?

DR. BURDON: I would be very glad to have the opportunity to tell you. We were fortunate enough to be in on an outbreak about sixteen miles outside of Houston in which an ear was sent to the city laboratory and we isolated B. anthracis, we then went out there right away to see what was going on. A total of sixteen animals died. This herd of more than three hundred cows had not

been vaccinated for two years.

We got out there just a few moments after the carcass of the first cow that died had been taken away, but the farmer, a very intelligent fellow, had gotten his farm wagons around and had isolated this place in the middle of the pasture where the animal had lain. The animal died during the night.

There was some obvious blood from both the head and tail, where this animal had lain. We picked up that soil and took it back to the laboratory and we still had anthrax bacilli that was obviously contaminated from the dead animal. Then we collected from the farm all sorts of material including soil from that pasture and from one across the way where no animals had died, and several samples of feed. It looked like there are all sorts of opportunity for this material to be contaminated because he had these boxes of feed on an open floor there, but we have never succeeded in any one of these cases in getting anthrax bacilli. We did isolate the organism from the soil, but only in a case where there was obvious bleeding from the animal directly on to the soil. And I do want to say that some blood had been mixed with the soil.

May I make one more observation? We were there a little later when this thing went on. We saw an animal that had fallen over dead, within about at least seven or eight minutes after he had been so found out in the same pasture. We went out to see this animal and we noticed that there was no bloating. There was no discharge from the rectum or mouth or nose on to the soil.

We asked the workers around and they said, "Oh, yes, that is what happens." Only after the carcass has laid around for several hours and is bloated and so on that the pressure of gases from inside the carcass will cause exuding of blood at the open ends, and contamination of the soil.

I thought that very interesting. If the carcass could be taken to a ren-

dering plant early enough, it might be that contamination of the soil would not occur. I would like to have someone else tell me whether that makes sense or not.

DR. MORTON: I would like to ask Dr. Burdon a question -- whether or not he has tried the medium of Peirce and Powell. Of course, lysozyme is one of the ingredients in that medium and it is known that anthrax bacilli are sensitive to the action of lysozyme. It seems peculiar that they will willingly use a substance that is known to destroy the anthrax bacillus in the medium for the purpose of isolating that organism.

DR. BURDON: We didn't seriously consider it for that reason, but we are actually making some tests of stock cultures now to see how they work out.

DR. MORTON: Good.

DR. DAVIS: I would like to ask Dr. Burdon if he would like to comment on the Ascoli test and whether he feels it is sufficiently sensitive to be useful in the diagnosis of anthrax in animals.

DR. BURDON: The only man whom I ever met who used the test is a somewhat elderly gentleman at A. & M. College who said he used to do the test years ago. I have had no experience with it. You would have to have a high-powered serum. Whether it is available I don't know.

DR. MORTON: Has anyone had any experience with the Ascoli test?

DR. STEIN: A number of years ago we tried the Ascoli test on cases of suspected anthrax in livestock and we found it was a non-specific reaction. In other words, organisms such as anthrax-like organisms, B. cereus, B. subtilis, and other organisms of that type may give you a reaction to the Ascoli test. You may also, of course, get a reaction with B. anthracis, but with a positive Ascoli test we always check and confirm the Ascoli test by culture and laboratory animal

inoculation.

In recent years there have been a number of writers throughout the world who are of the same opinion, that the Ascoli test is not strictly a specific test for B. anthracis.

While on my feet I might say that for the diagnosis of anthrax in livestock the Department of Agriculture will not make a diagnosis on a microscopic examination nor on a culture test. They both, or either one of them, must be confirmed by animal inoculation. In other words, we must produce the disease in guinea pigs.

I might also say that we prefer the use of guinea pigs rather than mice. We know that if mice are inoculated with organisms similar to B. anthracis, particularly if you are handling a contaminated specimen, the mice will often die and show a lesion similar to anthrax. Even the blood smear may show organisms which might be confused with B. anthracis. So we prefer the use of guinea pigs which are highly susceptible to anthrax and which show very, very typical lesions.

Anybody who is familiar with anthrax in laboratory animals and has examined a lot of guinea pigs will very rarely make a mistake on the autopsy examination alone.

DR. MORTON: It is my understanding that Dr. Ascoli recommends the use of an organism other than the anthrax bacillus for producing immune serum. If you do not use anthrax bacilli as the antigen it is difficult to see how the reaction is going to be specific for the anthrax organism.

Are there any other comments?

DR. STEIN: I would like to make one more comment regarding the diagnosis of anthrax in livestock. Of course, we are interested in getting as

prompt a diagnosis as possible and it is not difficult to make a diagnosis of anthrax if one is familiar with the disease, providing you get an uncontaminated specimen. Unfortunately most of the specimens which we receive from different parts of the United States -- a great majority of them are contaminated with other organisms. It makes it rather difficult and it's not an easy matter by any means to diagnose anthrax and do it rapidly with such a specimen.

Furthermore, our work with anthrax, while principally concerned in the diagnosis of the disease in livestock, also includes industrial specimens -- bone meal, dust, soil, and so forth. It's very difficult to isolate anthrax bacilli from such material. Take, for instance, a shipment of bone meal which is likely to be contaminated with anthrax organisms. The very small sample that it is possible to examine bacteriologically may be negative while other protions of the immense load will probably be contaminated with anthrax bacilli. So when you have a negative finding after an examination of bone meal, it is questionable whether the entire load was negative.

Another thing: As previously mentioned, in examining samples of industrial materials, they are very apt to be highly contaminated with anerobes and anthrax-like organisms. Consequently, it is necessary very often to treat the samples with chemicals before going into your plating and animal inoculations.

Another method of isolation which we use is the scratch method. In other words, in a contaminated specimen -- we know it is contaminated by microscopic examination -- we will inoculate the animal on the abrasion produced on the abdomen. One handling anthrax material should always remember never to inoculate interperitoneally because if anything is there other than anthrax bacilli, particularly in mice, you're very likely to produce an infection and confuse the picture as far as anthrax is concerned.

DR. MORTON: Dr. Foter, do you have anything to add about the sterilization of wool?

DR. FOTER: There are two questions which I want to ask Dr. Steele. Dr. Burdon has indicated the multiplicity of tests that should be made to differentiate between B. cereus and B. anthracis. Dr. Steele, in discussing the English system of processing incoming materials indicated that the incoming material was examined before the processing and then sterility tested afterwards. In view of Dr. Burdon's comment, my point being, in the examination of the material before processing in Liverpool do they actually examine the material for B. anthracis or is it just a total count that they are getting before and after sterilization?

Furthermore, he discussed in his paper the English system of processing. I wonder if he has any comments on progress being made or reports on the efficacy of formaldehyde gas or ethylene oxide and carboxide mixture. Is that being used anywhere?

DR. STEELE: In regard to the first question, the laboratory at the Liverpool School of Tropical Medicine was using both the plate culture and the guinea pig inoculation methods. They were very conversant with all the other organisma that would simulate the anthrax bacillus. Dr. Koo, who was at Cambridge University at that time working on a thesis on anthrax and related organisms, was doing work at Liverpool (this was in 1949) and I would say on the basis of their experience that they would certainly be eliminating other organisms which would not be B. anthracis.

In regard to your second question, I am not familiar with the gaseous processes being used any place in the United States or in the world, for that matter. Maybe Mr. Yaffee has some comment on that.

MR. YAFFEE: I don't have any comment to offer on that last point. Dr. Steele asked me to say something about an earlier question regarding whether it would be economically feasible to have each individual plant put in its own sterilization process.

That, again, is very difficult to answer. I think that generally speaking a large scale operation might be more economical than a small one. On the other hand, the individual plant might have less expense from the standpoint of other administrative costs and overhead and things of that sort, so the costs might be comparable.

Competition is so important in industry and there is competition for the use of different materials, and it is quite obvious to us what is happening. Many of the large carpet manufacturers practically quit making wool carpets entirely of wool and I think if they were faced with the proposition of having to spend a few cents more per pound to sterilize the wool, they would just go over completely to the use of synthetic fibers. They're doing it anyway, I think, for other reasons, but it would just encourage them to do that.

DR. MORTON: Any other comments?

MR. WILLARD: Dr. Steele, in regard to that southern state you mentioned that was so perturbed about a case of anthrax, have you any information on how many plants have anthrax exposure in the state? Did they just single out this one plant?

DR. STEELE: I have no information as to how many plants they had in the state that would be handling animal fibers that may be contaminated with anthrax organisms. This case was reported to the local Health Department and inasmuch as it was the first time that anthrax had been reported in the community there was quite a disturbance about it. It was referred to the State Health Depart-

ment and they in turn referred it to the Public Health Service to ask advice on how they could manage it.

DR. KRAVITZ: At the time that case occurred there was only one plant of that kind in the state. That was the first plant. Whether others have appeared subsequently I couldn't say. This was about two years ago.

DR. KRAMER: I would like to inquire whether this same industrial hazard exists in other plants using bone and animal carcasses, such as gelatine manufacturers. Is there a similar hazard there?

DR. STEELE: There is a paper published in The Lancet a couple years ago about an industrial outbreak of anthrax in a bone crushing plant in Wales. That is the only one that has come to my attention in recent years. I can't think of anything in the United States.

Dr. Stein, do you recollect any experience in the United States where there has been human anthrax in bone crushing plants or fertilizer plants?

DR. STEIN: No, I don't know of any.

DR. STEELE: The only one I can think of is that one in Wales a few years ago. That article carried a few references, but I can't recollect any of the references. They were also English and Continental experiences.

DR. KRAMER: One reason I asked the question is that I have from reliable sources a case reported in a New England State. That was only one case and it was very hushed up. I wondered whether or not anybody else had the experience with anthrax with these gelatine manufacturing places where they use a lot of this material.

DR. STEELE: There is another one in New England in an ivory plant, where they handled ivory tusks. There have been a few reported in the fur industry in this country both on the farms where minks are being raised and the

fur cutters' shops and places like that. Then there is another exotic one about a Christmas tree being brought into a home and a child allegedly developing anthrax from that. I think those exotic things are always possible but you have to consider the survivability of the spore.

DR. MORTON: If there is no further comment, we will adjourn for lunch and reconvene at one-thirty.

RECESS

AFTERNOON SESSION

(The afternoon session convened at 1:30 o'clock P.M.; Dr. C. L. Wilbar, Jr., presiding.)

DR. WILBAR: This afternoon we are going to have two groups of papers, one on the pathogenesis of anthrax, with a discussion following that, and the last group on the treatment of anthrax cases. The first paper of the afternoon will be given by Dr. Wm. J. Cromartie, of the University of North Carolina, School of Medicine, Department of Bacteriology and Immunology. The doctor's paper will be on the "Pathogenesis of Cutaneous Anthrax". Dr. Cromartie.

THE PATHOGENESIS OF CUTANEOUS ANTHRAX

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Present knowledge does not allow a precise analysis of all the mechanisms of the host-parasite relationship relative to the development and resolution of cutaneous anthrax. However, sufficient data are available to permit an understanding of some aspects of this problem.

The circumstances that, under natural conditions, bring spores of Bacillus anthracis in contact with the skin are well understood. It is generally believed that the intact epithelium offers protection from this infection and that the spores usually enter the host tissue through breaks in the epidermis resulting from minor injuries.[1] The normal extracellular tissue fluids provide a suitable environment for the germination and proliferation of this organism. In experimental infection in a variety of animals, germination and proliferation were observed to occur as early as 2 hours after injection of spores. In the skin of the relatively susceptible species of animals proliferation continues as the lesion evolves until death terminates the process. In the skin of the relatively resistant animal the bacilli, after about four hours, stop multiplying and gradually disappear as the lesion heals. From these observations it is concluded that the extracellular tissue fluids of all the species tested initially support germination and proliferation of B. anthracis. Approximately four hours after injection of the spores, the quality of this fluid is changed in the relatively resistant host in such a manner as to lead to loss of capsule and disintegration of bacilli. In the relatively susceptible animal, progression of the

disease is closely related to continued multiplication of the bacteria in the extracellular tissue fluids and their dissemination throughout the body.[2]

Growth of B. anthracis in the skin is associated with changes in the structure of the adjacent tissue. The most striking features of the histopathological alterations are evidence of capillary damage and the accumulation of edema fluid which disrupts the normal structure of the collagenous connective tissue. As the lesion evolves, the overlying epithelium exhibits varying degrees of necrosis. The number of polymorphonuclear leukocytes infiltrating the lesion is few in the relatively susceptible host in which proliferation of organisms continues and large in the relatively resistant host in which proliferation stops. However, phagocytosis of the bacilli is not a prominent feature of this process.[2]

A degree of understanding of mechanisms that seem to control the extent of multiplication of B. anthracis in the extracellular tissue fluids has been gained by studying the anthracidal properties of a material that can be extracted from leukocytes and other tissue cells.[3] Electrophoretic and chemical analyses have shown this substance to be a basic polypeptide containing a large amount of lysine. The evidence indicating that this material is important in the natural resistance to anthrax infection is all indirect. The production of large amounts of capsular material by the infecting organisms is a characteristic of progressive anthrax lesions. It has been observed that the effect of this anthracidal material is completely neutralized by the capsular material of B. anthracis which consists of glutamyl polypeptide. These observations, taken together, permit one to speculate concerning the possible role of capsular material and the anthracidal substance in the pathogenesis of this infection.[4] If one assumes that the natural resistance of a host rests on the ability to mobilize the anthra-

cidal material and that the survival of the parasite is dependent on the production of capsular material which neutralizes the anthracidal material, the outcome of an infection would in part rest upon the quantitative relationship between these factors.

The observations that progression of this disease is closely correlated with the multiplication of B. anthracis in the tissue fluids does not make clear the mechanisms that operate to cause the production of tissue damage, the clinical picture of the disease, and death of the host. Many efforts have been made to isolate a toxin from cultures of B. anthracis without success. The idea that the large number of bacterial cells in the blood produced a state of anoxia has been advanced as a cause of death in this infection but has not been substantiated. Mechanical capillary obstruction by masses of these organisms has been suggested as the most likely cause of death; however, evidence is lacking to support this concept.[2] Studies of sterile extracts of anthrax skin lesions demonstrate the fact that these extracts are capable, on intracutaneous injection, of producing histopathological changes comparable to those produced by infection with B. anthracis.[5] Further studies suggest that the tissue damaging property of these crude extracts is associated with the capsular material produced in vivo. Although the capsular material produced in vivo is chemically similar to glutamyl polypeptide produced in vitro, the in vitro produced material does not exhibit the tissue damaging property. This observation would tend to explain the failure of many workers to isolate toxic materials from cultures of this organism. The mild tissue damaging property of sterile filtrates of exudates produced by infection with B. anthracis has been confirmed by the recent studies of Keppie, Smith, and Harris-Smith.[6] The role of the material responsible for the local tissue damaging effect in production of death from this disease has not

been established. It has been suggested by Keppie, et al,[6] that once the organisms are able to grow freely in the extracellular tissue fluids, death of host could result either from the combined action of a number of mildly toxic substances or through the host's tissues being deprived of essential metabolities by the metabolic activity of the bacteria. The capsular material produced in vivo, as well as producing a mildly toxic effect on the skin, has been shown to be capable of interfering with the blood clotting mechanism. Fatal anthrax infection in rabbits is associated with a disturbance in carbohydrate metabolism as evidenced by hyperglycemia. The terminal picture of fatal infection in rabbits suggests that calcium metabolism might be interfered with and the injection of calcium salts tended to protect rabbits from the pathogenic action of this organism.[7] From the available data one can only conclude that much more information will have to be gained before a clear understanding of the mechanism of death in this disease will be possible. The data available do suggest lines of investigation that might be of value.

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DR. WILBAR: The next paper will be given by three gentlemen: Drs. Walter J. Levinsky, T. G. Anderson and G. Richardson, of Temple University School of Medicine, Departments of Medicine, Microbiology, and Pathology. The paper will be on "A Possible Case of Inhalation Anthrax" and will be presented by Dr. Levinsky.

INHALATION ANTHRAX MENINGITIS AND BACILLEMIA

A Case Report

By

Walter J. Levinsky, M.D.

Theodore G. Anderson, Ph. D.

and

Gail R. Richardson, M.D.

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The respiratory pathogenicity of B. anthracis spores in animals is well documented. In mice, guinea pigs, sheep, and rabits, spontaneous and fatal anthrax infections are produced experimentally via the respiratory route, both by inhalation and by intranasal instillation. To the best of our knowledge no fatal human infection of B. anthracis has been reported where the portal of entry was via the respiratory route without evidence of a local lesion in these structures. We recently had the opportunity to study a fatal case of this disease in which we believe the causative organism gained entry by this route.

CASE REPORT

This 37 year old white female was admitted to the Temple University Hospital in a semi-comatose state. The history, as obtained from her husband and the referring physician, disclosed that the patient was in excellent health until five days prior to admission. At this time she had the onset of malaise, mild fever, and dull pain in the low back and the posterior aspect of both legs. She was given analgesics and symptomatic treatment with no apparent benefit. Two days prior to admission, the husband noted that she appeared restless and would pace the floor excessively, but stated she denied any particular complaints other than general malaise, loss of appetite, and a mild headache. On the day of admission, she again complained of a headache. She had one episode of vomiting, then gradually became lethargic and unresponsive and was brought to the hospital.

Close questioning failed to disclose any history of preceding infection, trauma, tooth extractions, injections, animal contacts, or other possible precipitating causes for the present illness. The past medical history was unrevealing.

The physical examination revealed a toxic, semi-comatose white female

who responded only to painful stimuli. The temperature was 104.6°F., the pulse was 120, and the blood pressure was 120/68. The head was deviated slightly to the left and the eyes were fixed in an upward and lateral gaze. There was moderate nuchal rigidity. Slight weakness and increased deep tendon reflexes were noted in the left upper extremity. A soft systolic murmur was audible over the precordium. The oral and nasal cavities, ear canals, chest, abdomen, and genitalia were negative. The skin was clear and the remainder of the physical examination was essentially negative.

A lumbar puncture disclosed an initial pressure of 400 mm. of water. The spinal fluid was turbid, slightly xanthochromic, and contained 4,440 cells per cubic millimeter, all of which were neutrophiles. Direct smears of the spinal fluid were teeming with large numbers of gram-positive bacilli which were arranged in chains. (Fig. 1).

The patient expired one hour after admission and before any definitive therapy could be instituted.

NECROPSY

Post mortem examination was performed by Dr. G. R. Richardson two hours after death. The pertinent gross findings consisted of small bilateral pleural fluid collections, moderate ascites, and slight congestion of the upper lobe of the right lung. The spleen was enlarged, soft, flabby, and weighed 450 grams. The mesenteric, retroperitoneal, peritracheal, and mediastinal lymph nodes were moderately enlarged, dark red in color, and moderately firm in consistency. There was no peripheral adenopathy. The adrenals, kidneys, and pelvic structures were grossly normal. The meninges were cloudy and the vessels on the surface of the brain were moderately congested. Several tiny collections of thick tenacious exudate were noted at the base of the brain.

The remainder of the gross examination was unrevealing.

Histologic studies showed a mild diffuse interstitial pneumonitis and marked reactive hyperplasia of the mediastinal, peritracheal, retroperitoneal, and mesenteric lymph nodes. A few acute inflammatory cells were noted within the walls of the Fallopian tubes and in the endometrium, which was in an early secretory stage. The meninges were involved in an intense acute inflammatory reaction characterized by focal collections of polymorphonuclear leukocytes. Numerous large rod-like bacilli could easily be identified within the inflammatory exudate. (Fig. 2).

BACTERIOLOGIC STUDY

Direct smears of the spinal fluid showed profuse numbers of large gram-positive sporulating rods which were arranged in chains. The pre-mortem and post-mortem blood cultures and smears from the leptomeninges also disclosed large numbers of similar organisms. Lengthy and detailed bacteriologic and animal inoculation studies by Dr. T. G. Anderson and Dr. K. L. Burdon[4] established the organism as virulent B. anthracis.

DISCUSSION

In the present case there was no apparent cause or precipitating factor whereby the B. anthracis could have been introduced either into the blood stream or into the cerebrospinal fluid other than by ingestion or inhalation. The dermal surfaces were intact, there were no recent injections, extractions, lacerations, or contact with brushes, animals or other likely causes for the initial infection. By exclusion, the respiratory route of entry appears most likely.

Much work has been done on respiratory anthrax infections.[1,2,3,] Buchner[5] first studied experimental infections in animals with air-borne an-

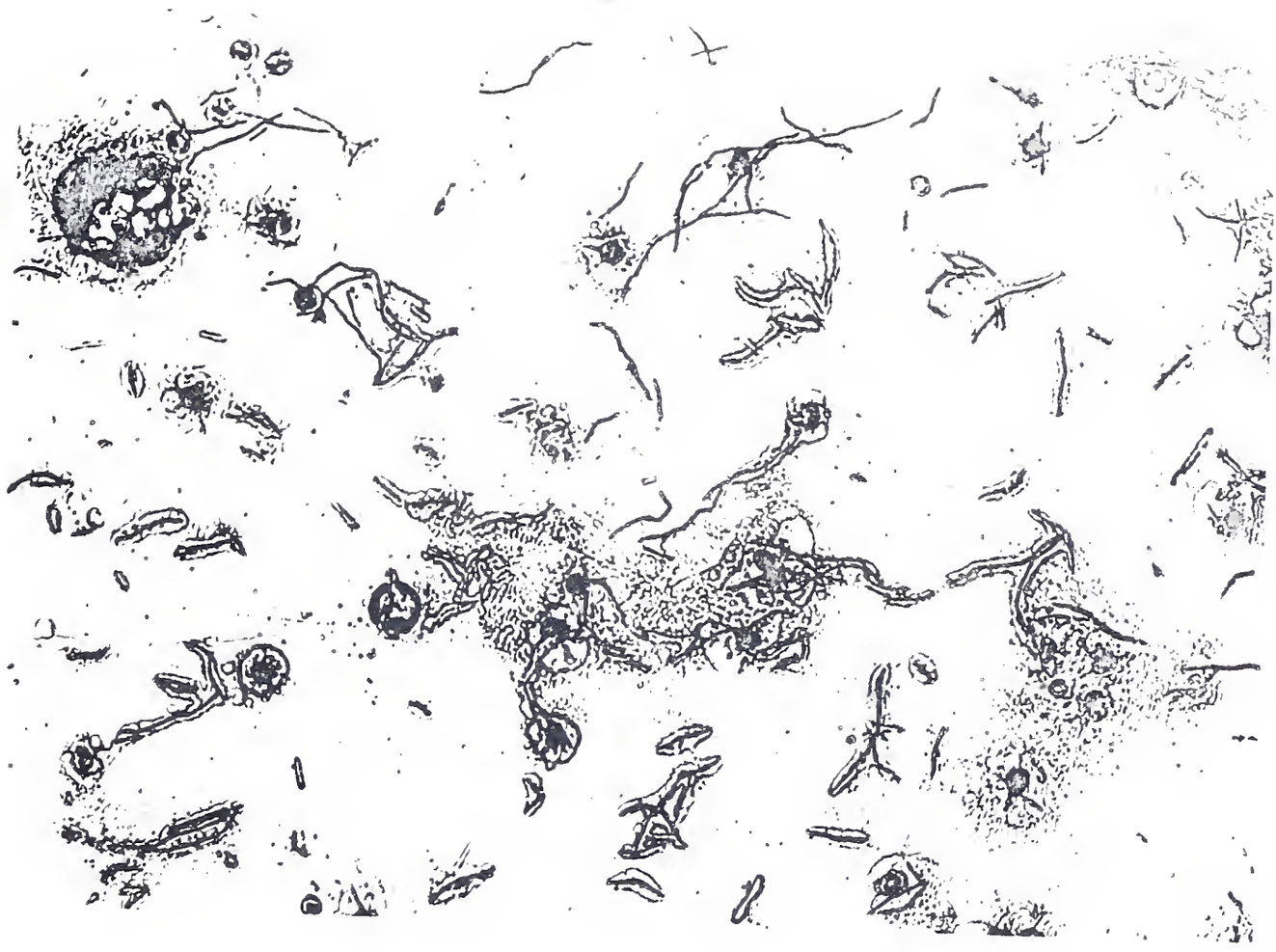

Fig. 1. Smear of spinal fluid

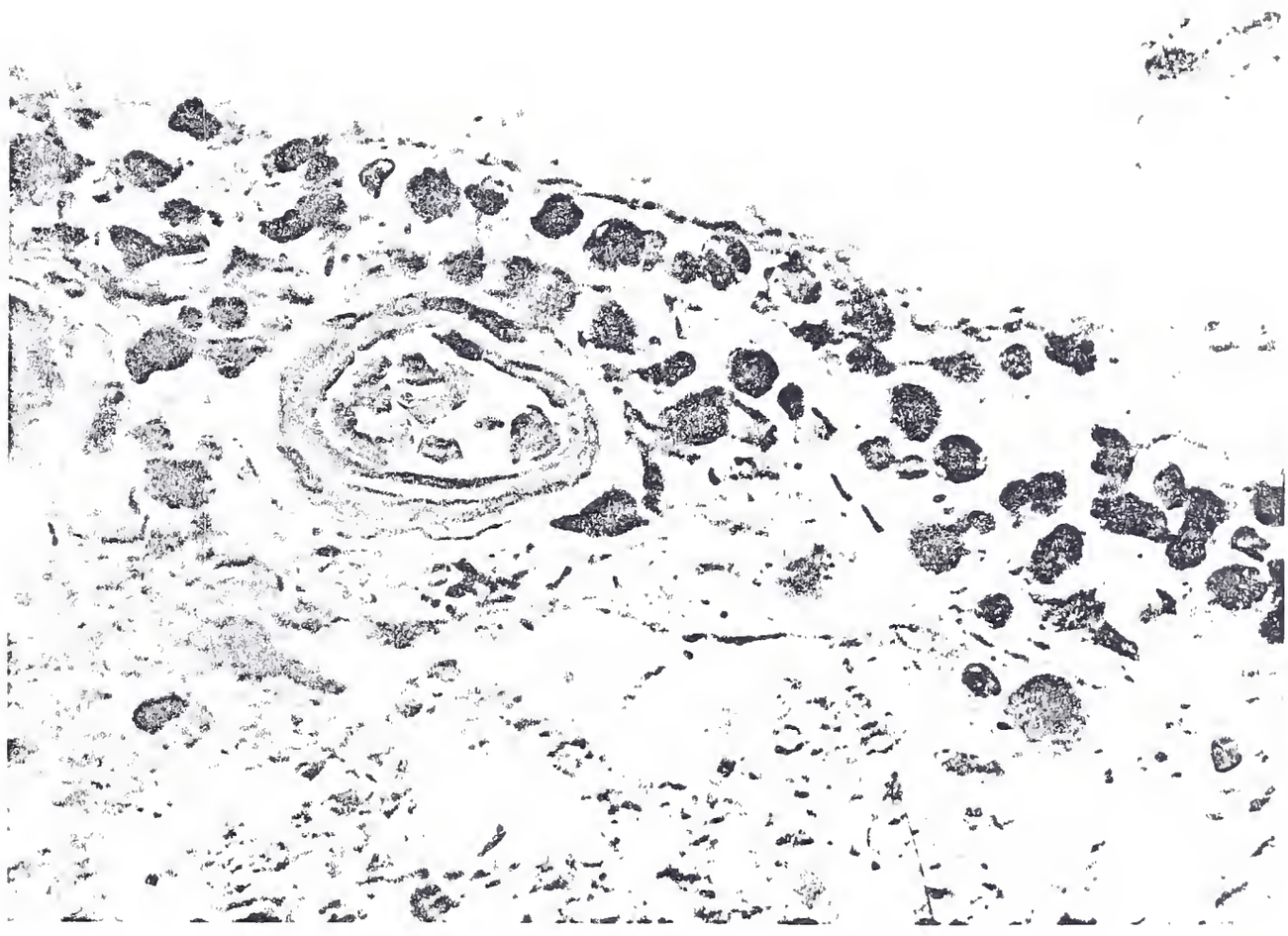

Fig. 2. Section of meninges showing inflamatory exudate and B. anthracis

thrax spores as early as 1888 and his original work has since been confirmed by many other investigators. It was shown that anthrax infections could be introduced through normal lung epithelium. Intranasal instillations of anthrax spores were also found to cause infections in guinea pigs.[6] Others found that lungs damaged by inhalation of chlorine gas greatly facilitated the establishment of respiratory infections.[7]

Detailed histopathological studies in several animal species indicate that respiratory exposure to anthrax spores results in a general infection rather than a primary pulmonary disease. The pulmonary system acts as a site of invasion, the organism being then transported elsewhere to multiply, then resulting in a bacillemia which characterizes fatal anthrax infections. The initial site of invasion of the spores cannot be determined histologically and it has been shown that there is little or no inflammatory reaction of the pulmonary tissues to inhaled anthrax spores until a few hours prior to death, and terminal bacillemia is accompanied by minimal changes only.[1]

The gross and microscopic autopsy findings in this fatal human case of meningitis and bacillemia due to B. anthracis disclosed a mild diffuse interstitial pneumonitis and marked reactive hyperplasia of the mediastinal and paratracheal lymphatic structures simulating the findings noted in experimental inhalation anthrax studies in animals.

CONCLUSION

A fatal case of bacillemia and leptomeningitis due to B. anthracis is presented. It is believed that the portal of entry of the causative organism was via the respiratory route.

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DR. WILBAR: I don't know how this conference could ever have happened or progressed so well without Dr. Morton. He helped to arrange the program, obtained the meeting place, presided at the morning meeting, takes care of the stage effects, and now he is going to present a paper on the "Pathogenesis of Inhalation Anthrax." Dr. Harry E. Morton, Professor of Bacteriology of the University of Pennsylvania, School of Medicine.

PATHOGENESIS OF INHALATION ANTHRAX

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The term "inhalation anthrax" is used in preference to the term "pulmonary anthrax" because it connotes that the infection was acquired by inhaling the infectious material. It has been demonstrated that practically the entire respiratory tract is susceptible to infection by the anthrax bacillus. From such primary foci of infection the organisms usually invade the body to produce a generalized infection. Death is the usual outcome of such cases. When anthrax bacilli enter the skin and produce an infection in the host there is a characteristic local lesion and adenopathy of the regional lymph nodes draining the infected area. With such criteria for the point of origin of anthrax infection, let us examine the published reports of anthrax infection in the respiratory tract of man.

A. Nasal Cavity

The nasal cavity is one region of the respiratory tract where anthrax bacilli might be introduced mechanically, as by manipulation with the fingers, or by inhalation. Air-borne material, especially large particles, may be trapped in the nose because of the architecture of the cavity. Infections in the nose are especially serious because of the high vascularity of the region, the abundant nerve supply, and the close proximity of the region to the brain.

Risel in 1903 described a fatal case of anthrax in which the primary infection was in the nasal mucous membrane of the superior conchae. Anthrax bacilli were quite abundant in this area. The trachea, bronchi, and lungs showed no important changes, and anthrax bacilli could not be found in the lungs. Risel concluded that the infection spread from the nasal cavity to the meninges by way of the perineural lymph channels of the olfactory nerve. There was also a lesion about 11 cm above the ileocecal valve in which the epithelium was absent. B. an-

thracis was present in the lesion and also in a small mesenteric gland. In a footnote to his article Risel stated that Schmorl had reported a case of anthrax in which the infection started in the nose and developed into diffuse hemorrhagic infiltration of the meninges.

Eurich (1933) observed 3 cases of anthrax infection of the upper respiratory tract, and in one case the infection affected the nasal passages.

Inda, Natin, and DaRin (1943) reported a case of inhalation anthrax in which the primary local lesion appeared in two locations - in the nasal region and in the upper surface of the soft palate.

Here in the Philadelphia area Krauss in 1943 described a fatal case of anthrax infection in which the nasal passages on both sides were completely blocked. B. anthracis was isolated from the nasal secretions and from the blood. This case also showed a lesion in the intestinal tract.

B. Pharyngeal Region

The pharyngeal region is another area of the respiratory tract in which, because of the curvature of the walls, large air-borne particles may be trapped. Eurich (1933) described 2 fatal cases of anthrax in man involving the pharyngeal region, one affecting the right tonsil and the other affecting the tissues between the epiglottis and the glossopalatine arch.

Vaccarezza and his coworkers, who have emphasized the importance of primary anthrax carbuncle of the pharynx, described a case in which the lesion was located on the midline of the posterior wall of the pharynx midway between the oro- and naso-pharynx. After the pharyngeal edema subsided, posterior rhinoscopy revealed a rounded ulceration covered with necrotic tissue (Vaccarezza and Peroncini, 1938). There was submaxillary and retromaxillary adenopathy.

marked edema of the neck, the lower part of the face, and the pharynx. Anthrax bacilli were cultured from the nasal and pharyngeal secretions and from the blood. There were constipation and bloody stools. The authors concluded that this was a case of primary infection of the posterior wall of the pharynx which gave rise to septicemia and manifestations of secondary infections in the intestinal tract. Eurich (1933) expressed the opinion that generalization of the anthrax infection is due to emboli as judged by the distribution and structure of the secondary intestinal lesions in cases of pulmonary anthrax, the emboli being derived from thrombosed veins in the area of the primary focus. In another case (Vaccarezza and Vivoli, 1939) the lesion developed on the left tonsil. When the lesion appears on the tonsil there is the possibility of a mistaken clinical diagnosis of diphtheria, as happened in this case. In the subangular maxillary region there was a swelling the size of a small orange containing engorged lymph nodes. There were lesions also in the intestinal tract.

Vaccarezza stressed the similarity of pharyngeal anthrax in man to that of swine, which is the type of infection commonly encountered in that species.

This brings to mind some work of Wood from this Medical School in 1914. In an attempt to determine the importance of the tonsils as a gateway for cryptogenic infection, Wood selected swine as the experimental animal because this species possesses a tonsillar structure sufficiently large and accessible. B. anthracis was selected as the test organism because of its known pathogenicity for swine, its ease of cultivation, and the readiness with which it can be stained in tissues. In one hog the culture was rubbed on the surface of one tonsil and a lesion developed only on the other tonsil. This illustrates the point that infection will develop only when the conditions are right for its development.

What these conditions are remains pretty much in the realm of Nature's mysteries.

MacDonald (1942) reported an interesting case of fatal anthrax from Massachusetts. The author reported it as involving the cutaneous and gastrointestinal systems. The involvement of the respiratory tract was referred to incidentally. The patient was seen at home by his physician because of sore throat and swollen lymph nodes on the right side of the neck. Some days later the patient was admitted to the hospital in a very critical condition, with a tentative diagnosis of mumps. In the meantime a pustule on the forehead had aroused the suspicion of the physician. The patient died 6 hours after admission. There were 6 lesions in the intestinal tract. Before death, it was observed that thr roof of the mouth was studded with 8 to 10 tiny yellow pustules. At autopsy the pharynx was red and injected and a heavy, greenish-yellow exudate was noted in the post-nasal space. MacDonald pointed out that the mode of invasion of the gastrointestinal tract was undoubtedly the swallowing of large numbers of spores. The fact that the patient first complained of a sore throat and swollen cervical lymph glands suggests the possibility of the anthrax infection's originating in the region of the pharynx. The lesion on the forehead may have been the result of mechanical transfer of organisms from the nasal or oral secretions to that area. From the observations of McCurrich (1920) and Cromartie, Bloom, and Watson (1947) on the development of local lesions, it is quite possible that the carbuncle on the forehead developed after the infection started in the throat. Anthrax bacilli were demonstrated in the blood before and after death, and in materials from the forehead and from fluid in the peritoneal cavity at autopsy. Unfortunately no mention was made of examining the material from the pharynx, so that the exact

interpretation of the case has to remain in doubt.

Inda, Natin, and Giuliano (1947) described a case of pharyngeal anthrax in which the symptoms of infection began at the level of the neck of the fauces.

C. Oral Region

It is possible for the oral cavity to become contaminated with B. anthracis. This may come about by inhalation or by ingestion. The oral bacterial flora is more apt to resemble that of the pharynx than of any other region of the respiratory tract, a point brought out by Williams, Appleton, and Polevitzky (1952) of the Dental School of the University of Pennsylvania. One case of anthrax of the oral cavity was described by Briggs (1947) in a patient in Indiana. The infection first appeared in the left half of the hard palate.

D. Laryngeal Region

Evidence of primary and sole infection of the larynx is lacking. Eppinger (1894) described a case in which there was a small area near the pharyngo-laryngeal junction which was devoid of epithelium and the muscous membrane of the larynx and trachea was slightly swollen, reddened, and interspersed with single ecchymoses and nodule-like foci up to 1.5 mm. in size. Both bronchi were somewhat swollen and reddish purple in color. Both lungs contained less than the normal amount of air and the bronchial lymph glands were enlarged, soft, pulpy, dark colored.

E. Trachea

The trachea, being a fairly straight tube of a few inches in length, does not afford much opportunity for particulate material to impinge upon its walls during breathing. Nevertheless, Risel (1903) pointed out that, in the case of anthrax in a man who worked at a threashing machine reported by Marchard (1894),

there was a local lesion in the middle of the trachea on the anterior wall. At the right side of the trachea and at the right bronchus there was an extensive cluster of greatly swollen lymph glands. Below the bifurcation of the treachea there was a second similar and very extensive cluster of lymph nodes.

Popov (1914) stated that Yasinski published an account in 1911 of a case of primary anthrax in the mucous membrane of the trachea above the bifurcation.

F. Bronchi

Lodge in 1890 stated that anthrax infection in woolsorters takes place by direct inoculation by spores on some part of the bronchial tree, generally the large bronchi as far as the second division. In typical cases one found the bronchial lymph nodes to be hypertrophied and injected, there was a bronchopneumonia without special character, and a septicemia was evident. In the submucous tissues in the trachea and bronchi, at the level of the hemorrhagic extravasations, masses of anthrax bacilli were found in the lymph spaces around the blood vessels or as a generalized invasion of the glands. These typical findings were verified by Risel (1903) from the autopsy of a case in which the local lesion was located in the left bronchus about 2 cm below the bifurcation. Microscopic study of the lesion showed it to be a small anthrax pustule. The lungs were also affected in this case.

The fatal case of bronchial anthrax reported by Shennan and Miller (1909-1910) illustrates the susceptibility of the human respiratory tract to infection with B. anthracis. At the bifurcation there was a deeply congested area extending upward for about 1.5 inches and downward into the bronchi past their first divisions. A small greyish-yellow patch, the size of a hemp-seed, evidently of necrotic nature, was observed in the left bronchus just below the bifurcation. The lymph glands about the bifurcation were greatly enlarged

and infiltrated with blood; those at the root of the lungs and along the bronchi and trachea were to a great extent disorganized. Bacilli were present in large numbers and were especially grouped at the periphery, being evidently collected in the sinuses. The lungs were also affected, and bacilli were especially evident in the hemorrhagic areas, but no bacilli were found within the blood vessels.

Popov (1914) described a fatal case of anthrax in a laboratory worker. The mode of infection was thought to be by inhalation; the point of entry appeared to be the left bronchus, and death was produced by septicemia.

Fraenkel (1925) emphasized that the region of the bifurcation, especially the spur and adjacent areas of both bronchi, must be considered a favorite spot for the portal of entry of the anthrax organism. He presented the results of five cases in support of his contention.

G. Lungs

It is estimated that in the two human lungs there are on the order of 6,000,000 air sacs, and the surface shared by lung and air is about 900 square feet. It is well known that airborne particles less than 5 microns in diameter readily enter the lungs during breathing, and a goodly proportion of the particles are retained therein. Because of the structure of the lungs, it is not possible to search for and find therein a local carbuncle and establish the portal of entry as can be done for the remainder of the respiratory tract. Areas of consolidation in the lobes, hemorrhagic infiltrations, edema, and other signs readily indicate lung involvement. If anthrax spores or anthrax bacilli pass through the walls of the alveoli, by diapedesis or otherwise, they may enter the lymph or blood, or both. If the organisms enter the lymph, there will be involvement of the draining lymph nodes. The hilar, bronchial,

tracheal, and mediastinal nodes have been described as showing massive involvement. The regional lymph nodes may not necessarily be involved, as it has been stated that some lymphatics in the lungs pass directly into the thoracic duct (Miller, 1938). If the organisms enter the blood the lymph nodes throughout the body may be affected. Both lungs have shown about equal frequency of involvement, so that it is reasonable to assume that the infectious material entering the lungs is in a fine state of suspension.

Rembold in 1879 reported two cases of ragsorter's disease. In one case the seat of the pulmonary disease was in the lower portion of the right lung. Anthrax bacilli were detected in the blood. The patient recovered, which is unusual. Mortality from inhalation anthrax is usually estimated to be about 90 percent. The other case terminated fatally. The lungs and pleura were affected, and anthrax bacilli were not detected in the blood prior to death.

The case reported by Poland (1886) represents the rapidity with which death may occur in the absence of specific treatment. The man worked only one day among dry hides which gave off clouds of dust when handled. Six days previous to this he had done no work. The symptoms developed rapidly on the third day after this exposure, with death following within 15 hours. Poland was unable to demonstrate anthrax bacilli, but even with our present day bacteriological methods LaBoccetta (1948) stated that of their 36 human cases of external anthrax the diagnosis was not confirmed bacteriologically in 16.6 per cent.

Eppinger (1894) gave very good descriptions of the autopsies on 11 cases of ragsorters' disease. Petroff (1897) described a fatal case of anthrax acquired by the respiratory tract in a brush maker. From his microscopic studies, he concluded that the anthrax bacilli disseminated principally by way of the lymphatics

of the lungs. Schottmueller (1898) also described 2 interesting fatal cases of inhalation anthrax.

Cowdery (1947) reported a fatal case of primary pulmonary anthrax, with septicemia, occurring here in Philadelphia. The individual began cleaning some new rugs prior to selling them. The hilar and mediastinal lymph nodes were enlarged, hemorrhagic, and black. The lower lobe of the left lund contained no air, was gelatinous and homogeneously blackish red in color. There were numerous secondary small superficial ulcers in the stomach, duodenum, jejunum, and ileum.

It is not known what specifically determines the level in the respiratory tract at which an anthrax infection may originate, but it is known that particles of different sizes are deposited in different locations. It is known that the size and mass of the particle determines the degree of penetration of air-borne material into the respiratory tract. Very few particles larger than 5 microns in diameter pass through the nose. From the standpoint of air-borne bacteria which penetrate the respiratory tract to the lungs, the particles probably have an average diameter of between 3.5 and 1.0 microns. Eisenbud (1952) clearly points out that it is the mass of a particle which is the property most likely to influence the site of deposition in the respiratory track and that, for air-borne particles of approximately equal density, the size of the particle then becomes the property most concerned in determining the site of deposition. Druett et al. (1953) demonstrated in experimental studies on guinea pigs and monkeys with aerosols of anthrax spores that the size of the particle and not the number of spores was important in producing lethal infections. The lethal dose for 12 micron particles was 14 to 17 times greater than for aerosols of single spores. Particles of sizes up to 5 microns in diameter were about equally infective. They

concluded that the lung proper is the most susceptible region of the respiratory tract for initiating infection. The exact method by which the anthrax spores germinate and produce a lethal infection is still an unsolved problem.

Summary

There can be no doubt about man's acquiring anthrax by the air-borne route. In many instances it is possible to determine the exact site of the primary infection.

Five cases have been reported in which the primary infection took place in the nose. In one of the cases the superior conchae was designated the primary site of the infection.

Six cases have been reported in which the pharyngeal region appeared to be the site of the primary infection. The right and the left tonsil were each named as the affected site; likewise, the tissues between the epiglottis and glossopalatine arch and those between the oro- and naso-pharynx on the posterior wall of the pharynx.

The oral cavity has been described as the primary and sole area of infection in one case.

No report has been found that the larynx was the primary and sole site of infection.

In two cases the primary site of infection has been reported in the trachea; once on the central portion of the anterior wall, and once above the bifurcation.

The bronchi have been involved so frequently that some authors have stated that the bronchi must be considered a favorite spot for the portal of entry of the anthrax bacillus.

The lungs are frequently involved. Either the right or the left, or both,

lungs have been involved and the involvement of the two lungs has been reported with about equal frequency.

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DR. WILBAR: Our stenographer suggests that it would facilitate the discussion if the speakers would stay on the platform during the discussion period, so we'll try that method this afternoon. I am sure some of you have some questions or comments on the subject of the pathogenesis of anthrax. If you haven't spoken this morning, would you please give your name when you rise. Who has a question on this subject?

DR. MORTON: I would like to ask Dr. Cromartie if he has any comments about this dermonecrotic toxin that has been reported by (I think it was) Evans recently, supposedly an exotoxin.

DR. CROMARTIE: I really can't comment on it with any degree of authority. I know that many attempts have been made to isolate toxins from the cultures, and I would like to say just a word about this question of whether this organism does produce a toxin or not.

I t seems to me that if it does produce a toxin, it must be a relatively mild acting agent. Otherwise you wouldn't expect the host to survive long enough for such a large number of organisms to be produced. So I don't believe that it is rational to believe that someone is going to isolate a toxin that will be as potent as something comparable to diphtheria or some of the other more classical exotoxins.

I think the fact that the host can survive with such a large number of these organisms present is indication that the organism doesn't produce an extremely potent exotoxin of the usual type.

DR. WILBAR: Is Dr. Anderson, the co-author of the second paper, here? Would you like to comment on that subject, Dr. Anderson?

DR. ANDERSON: I have no comment.

DR. STEELE: I would like to inquire of Dr. Levinsky what the appearance of the blood was in this fatal case that he described. In animals the blood is often dark and tarry and not coagulated.

DR. LEVINSKY: I can't answer that. I don't think that it was unusual, however.

DR. STEELE: Was there any indication that you may have had a nasal invasion?

DR. LEVINSKY: We took a culture from this patient thinking of a meningitis of the nasopharynx through the nose, and I think Dr. Anderson reported no growth on that.

I would like to ask Dr. Morton if he has ever heard of a case similar to this, where we were unable to find any primary site in the trachea or lungs. This is purely an hypothesis. Would you care to comment on that?

DR. MORTON: Yes, I believe there are cases which show very little involvement in the lungs, but I didn't cite those because that might not be good proof that there was entrance through the respiratory tract. I simply took cases where there was evidence of local involvement of the respiratory tract and the draining lymph nodes. The two would be pretty good evidence of the site of invasion.

We realize that sometimes with cutaneous lesions the organisms may enter the bloodstream and then localize in the lung, and you get lung involvement; but that is secondary. In all the cases I have cited, local lesions in the skin had been ruled out.

DR. WILBAR: It seems rather remarkable, doesn't it, Dr. Morton, that is these plants which we hear are so dusty, where wool and hair is processed and

there is so much dust in the air with spores, that there aren't more inhalation cases. Do you think that perhaps there are a number of mild cases that are not diagnosed and go by unnoticed?

DR. MORTON: I don't know about the mild cases, but in reading some of the accounts of the cases of woolsorters' disease in the last century over in England I noted that Lodge particularly commented upon the clouds of dust given off from the hides that were handled and remarked how the individuals coughed and how at the end of the day their respiratory tracts were so irritated, and involved that quite often the workers found it difficult to walk home, which was perhaps a mile and a half removed from the factory.

Possibly today the factories are better ventilated and there is not as much dust and irritating fumes as there were in the mills back in the last century.

DR. KRAVITZ: The other part of the answer to that question is the matter of particle size. These spores are probably on the dust and in the air, but they are in rather large particles. This is also aided by the rather high humidity in most of these plants and these spores and dust come down in extremely large particles and are undoubtedly filtered out at the tip of the nares where there is very little chance for infection.

DR. GOLD: I think those who see anthrax are struck by the fact that in this country there are numerous cases of cutaneous anthrax, but very few cases of pulmonary anthrax reported in contrast with the old literature in Europe and England where pulmonary anthrax was extremely common.

I think that it is probably a question of particle size, although I am not at all sure of it. In the last 20 years we have seen only one case of pulmonary anthrax, while in the same department we have seen a number of cases of cutaneous anthrax. That individual was working in the same surroundings and handling ex-

actly the same dusty material, which is just as dusty now when it arrives in this country as it was 50 years or 100 years ago -- perhaps a little bit worse because now, perhaps because of commercial reasons, they increase the weight apparently by adding dust.

Why that particular individual came down with pulmonary anthrax and none of his associates working in the same department did, I do not know. Perhaps it is the same reason why certain individuals working in the same plant for 20 or 25 years don't contract anthrax, and then all of a sudden they come down with a cutaneous type of infection. Time and again we have been able to culture anthrax bacilli from the bales of hair and from the machinery that they have been handling day in and day out for 20 odd years.

I think it is very striking that in this country we don't see the pulmonary type of anthrax, but we are still confronted with the cutaneous type of anthrax.

DR. WILBAR: Dr. Witte.

DR. WITTE: I wonder if Dr. Cromartie has any explanation as to the lack of cutaneous lesions, or at least the rarity of cutaneous lesions, in animals that develop anthrax in the field. I don't believe you see too many cutaneous lesions where it occurs naturally.

DR. CROMARTIE: I think one thing we have to keep in mind in discussing portals of entry and evidence of that is that actually if you get a severe enough infection, or if you give a large enough dose intercutaneously or subcutaneously, the susceptible animal will die before it develops any, or without developing any, lesions at the site of inoculation.

I think that one reason we don't see so much in the way of large lesions in livestock, for instance, is that they are more susceptible and, although the organism does enter the skin, it may produce an infection without any local reaction

at all. I don't think you can use the development of a local lesion as absolute proof of the portal of entry, but I think certainly that many of our animals which we do inject with overwhelmingly large inoculants would die without any evidence - any gross evidence - at the portal of entry.

DR. STEIN: I would like to comment on that point if you don't mind, on anthrax in livestock. We generally consider naturally occurring anthrax that which is picked up by animals on pasture. Anthrax of that kind is usually of alimentary origin. We do find what a lot of the old writers used to call external anthrax, particularly in cattle and in horses, and that may occur as a result primarily of the animal's being infected by a fly contaminated with anthrax, and especially by a bloodsucking fly.

There you have an external cutaneous form of anthrax which may remain in that condition for quite a long while and then finally become septicemic. In swine, of course, you have the local form of anthrax there, but it is confined mostly to the throat and the maxillary and submaxillary lymph glands and the tonsils.

But we do have two distinct forms of anthrax in livestock. A good demonstration of cutaneous anthrax, or external anthrax, is when a highly susceptible animal is given a very virulent spore vaccine. Some animals will react very severely.

So we do have, though it is fairly rare, the cutaneous form of anthrax in livestock, particularly in cattle and horses. In horses you might say that we have a sort of anthrax which will assert itself by subcutaneous swelling of the throat, the various structures of the throat and the glands. The intestinal tract and the spleen will not be involved. The animal may die of anthrax and you will not have any involvement of the intestinal tract.

Another peculiar thing which is pretty hard to explain: We have sometimes an animal which develops cutaneous anthrax with a myxedema, with immense pressure exerted on the lungs and the blood vessels. The animal will die indirectly of anthrax. You will not be able to isolate the anthrax bacilli from the heart, blood, or the spleen but you can isolate it from the edema. We do have cases of that type.

DR. WILBAR: Dr. Kravitz.

DR. KRAVITZ: I would like to hear a little more discussion on the ability of the anthrax bacilli to get into the alveoli of the lung and not cause pulmonary infection. I am wondering if Dr. Morton or Dr. Levinsky could elaborate on that. Are there comparable situations in bacteriology?

DR. MORTON: I think very little is known as to what happens in alveoli when spores settle on the walls of the alveoli. Of course, back in the last century when an animal died of anthrax, it was skinned in an effort to salvage something from the carcass, and the hide was very heavily limed. When bundles of these hides were opened up in the factory dust was given off and undoubtedly there was material of an irritating nature adhering to the spores. This material might have been lime or animal dirt. So you may have had a condition there where the spore, plus some irritating material adhering to it, was deposited on the surface of the alveoli, which might measure 900 square feet in area. Somewhere the spore might set up an irritation to the tissue and call forth the body fluids and germinate, or it might be phagocytized and carried into the blood or lymphatic circulation.

MR. WELLS: Have there been any reports Dr. Morton of experimentally atomized aerosols of anthrax cultures?

DR. MORTON: Yes, there have been a lot of reports on experimental

infection of animals by aerosols. The first experiment with aerosolization of cultures was done with anthrax spores by Buchner in about 1888, so it has been demonstrated ever since then that you could blow dry anthrax spores up into the air and rabbits and guinea pigs would inhale the spores and develop anthrax infection.

I have a terrible question to ask and I want to apologize before asking it. The anthrax bacillus was the first bacillus discovered to be the cause of infectious disease. It is the largest bacterium, and it is one of the easiest to grow, and yet it is quite difficult to diagnose sometimes. I would like to ask Dr. Anderson if he would care to state how long it took them to attach the name Bacillus anthracis to this culture. My humble apologies to you for asking this.

DR. ANDERSON: Since Dr. Burdon is here to back me up, I believe I got the final report a year and a half after we made the initial isolation. Dr. Burdon, I believe that is correct, isn't it about that time?

DR. BURDON: Well; it doesn't take a year and a half to do it. Now you've got me on the spot. However, I think it is proper to say that somewhere in the course of handling these cultures, which we received from Dr. Anderson, our old friend Bacillus cereus got mixed in. These mixtures are very easy to produce. We think of our sporebearers as contaminating other cultures, but sporebearing cultures are easily contaminated by other sporebearers, particularly if you have a laboratory where you have been working with them a good deal.

At any rate, some of the cultures did not produce death in animals and gave us hemolytic colonies, so we had to reisolate and retrieve and recover all those that were typical -- I mean culturally and otherwise by chemical tests -- and they were certainly virulent anthrax bacilli. So we had somewhere along

the line, whether it was at the beginning or somewhere else, the presence of the organism that could be distinguished as B. anthracis.

If you have a mixture you may not kill the animal or you may kill the animal and not recover the anthrax organism. That is the sort of thing I was talking about this morning in questions of this kind. However, the actual time spent in doing these tests was certainly not a year and a half.

DR. MORTON: The point I wanted to bring out was that not only was a considerable period of time required but an almost minor research project was involved in definitely identifying the anthrax bacillus as the causative agent of this fatal case of meningitis. Back a couple of years when there was an epidemic of anthrax in Ohio it was stated that it took three weeks to get the report that they were dealing with anthrax out of the laboratory. It illustrates the point that a lot of work needs to be done on the culturing of the anthrax bacillus and the bacteriological diagnosis of anthrax, the oldest known bacterial disease.

QUESTION: I want to ask Dr. Cromartie if he has any comments to make as to the relationship between the anthracidal substance and the peptides as announced. The other question is whether there are any studies that have gone on as to what is the difference between the polypeptides produced in vitro and in vivo?

DR. CROMARTIE: I will answer the last question first. The only evidence that we had of difference was in purely biological tests and the question was whether polypeptides themselves exhibited the biological difference or something associated with them. The only difference that we could demonstrate was the ability to produce an edemic reaction in the skin and the ability to prolong the coagulation time.

Regarding the nature of the so-called anthracidal substance, I think it is fairly well established now that these polypeptides can be extracted from almost

any tissue that has a high content of nuclei. We are working with the same material that Dr. Bowles has been working with, and that is tubercle bacilli which have a polypeptide that has a high glycine content.

We don't think there is much doubt that you can extract these substances which are bactericidal. I think the big question that remains to be answered is whether or not these substances actually play any role in natural resistance. I think it is interesting to note the fact that the course of an anthrax lesion is closely correlated with the production of capsular material, and this capsular material, including the glutamyl-polypeptides, will neutralize the effect of the anthracidal substance. There has been very little work done on attempting to isolate the antibacterial basic polypeptides from lesions at various stages. I think that might be of some value in deciding the role which they play by trying to isolate them from the lesions as the lesions evolve. Does the amount increase as the number of organisms increase? That is one possible approach.

DR. WILBAR: Let us have a ten-minute break now, and reconvene in just ten minutes.

Short Recess

DR. WILBAR: The next part of this session will be on the treatment of anthrax, and the first speaker will be Dr. Sheldon C. Kravitz of Baltimore, who will speak on "The Effect of Modern Therapy on the Clinical Features and Communciability of Cutaneous Anthrax". Dr. Kravitz.

THE EFFECT OF MODERN THERAPY ON THE CLINICAL FEATURES AND COMMUNICABILITY OF CUTANEOUS ANTHRAX

Sheldon C. Kravitz, M.D.
Baltimore, Md.

Recently, I had the opportunity of seeing a case of cutaneous anthrax in a thirty-six year old white woman who lived in Monroe, North Carolina. The case itself was quite typical, but its impact on this community was most striking.

The factory in which this lesion was acquired was the first of its kind in the State of North Carolina. It was actually a branch of one of your Philadelphia concerns which processes raw goat hair into a hair-canvas product to be used for interlining men's coats and jackets. The patient was employed as a spinner of this yarn and had been working for two months before she contracted the disease.

The illness began with a single maculo-papular lesion on the volar aspect of her left forearm. No attention was paid to it, and within 6 days the inital lesion had reached a diameter of about 3 cm. Her entire arm had become swollen, hot, exquisitely painful, and red streaking was visible. Extremely tender lymph nodes were noted in the axilla and supraclavicular region. The correct diagnosis was made by the plant manager who sent the patient to a local physician. The latter gave the patient one million units of penicillin intramuscularly while she was still in his office and then hospitalized her. In the hospital she received 50,000 units of penicillin every 3 hours and 1 gm of sulfadiazine every 6 hours. This treatment was continued for 2 1/2 weeks. The fever, edema, and cellulitis subsided within 4 days. A black eschar persisted for several weeks.

As soon as the diagnosis was made, hysteria sprang up everywhere in

the community. The local doctor advised the hospital staff that this patient was highly contagious and that anyone touching her might die. As a result, the patient was lucky to get her medication. Courage to culture the lesion did not appear until 6 days after treatment had been started. No positive cultures were ever obtained from the patient. The patient received general care in the hospital from her loyal, but petrified husband, who changed his will 3 times during her first week of hospitalization.

At the plant, mass walkout of employees was threatened. At a dramatic midnight meeting of all the plant employees, the plant manager demonstrated his disdain of anthrax by rubbing the raw hair on his skin and even ingesting a handful. This material, as well as dust and wool particles, obtained from practically every surface in the factory was found to be loaded with anthrax bacilli. The plant manager escaped infection.

With the advent of penicillin and the broad-spectrum anti-biotics, recovery from cutaneous anthrax has become the rule. I do not want to anticipate Dr. Gold's paper on results of treatment in this disease. I do want to say something of the clinical course of the disease, complications, and communicability.

It was well shown by Ellingson and his group in Frederick, Maryland, that despite prompt institution of appropriate therapy in cutaneous anthrax, a typical cycle of pathologic changes still took place. The initial pruritic red macule soon becomes elevated and within a day or two becomes vesicular. The vesicular fluid is either clear or opalescent, and it contains the anthrax organism. The vesicle may rupture, leaving a small ulcer, or may form a ring of satellite vesicles. In two to three days these vesicles become hemorrhagic in character. The surrounding tissue is usually indurated and erythematous. The absence of pain at the site of the lesion contrasts sharply with similar abscesses caused by

the common pyogenic organisms. However, edema, lymphangitis, and lymphadenitis can and do cause exquisite pain in the affected part. Atrophy of muscles and temporary neuromuscular weakness of the hand and wrist may follow extensive edema of the arm. The patient cited exhibited all of these changes.

Effective antibiotics sterilize the lesion. It has been repeatedly shown that these vesicles and ulcers are sterile usually within 24 hours after the onset of penicillin therapy. Despite this rapid sterilization, tissue destruction goes on, undoubtedly due to a necrotoxic or inflammatory factor elaborated by the capsule. Such a factor has been isolated by Watson et al. at Camp Detrick. The action of this factor has been compared to that of hyaluronidase. It has the property of damaging tissue, and enhances the spread of spores. This factor is also capable of interfering with the clotting mechanism and probably contributes to the hemorrhagic nature of the ulcer.

With sterilization of the ulcer in less than 24 hours, chances of developing a septicemia should be correspondingly reduced. Anthrax meningitis is the dread complication of anthrax bacteremia. The exact incidence of anthrax meningitis is unknown. About 100 cases have been reported in the literature. Seventy of these were analyzed by Haight. It was found that the skin was the portal of entry in 53 percent of the cases. Bacteremia was demonstrated in 70 percent of these cases. The average duration of anthrax meningitis is 2 to 4 days, and only two cases are known to have survived this complication. Several cases have been reported to have occurred while the patients were receiving penicillin.

The epidemiology and communicability of cutaneous anthrax can be summarized in a few words. The intact skin is said to be an effective barrier against

anthrax infection. Yet in many instances, including the case to which I have referred, it is impossible to obtain a history of or to demonstrate, a previous skin abrasion. Of the 25 cases reported by Ellingson, only 5 gave a history of previous trauma to the skin. Person-to-person spread of anthrax is almost unheard of -- and this was true even in the pre-antibiotic era.

An interesting problem in communicability arose in Monroe. There was concern among the local gentry that agricultural anthrax might be introduced via this contaminated factory. Veterinary and agriculture experts did not seem too perturbed by this possibility.

In summary, cutaneous anthrax is now a disease readily curable with penicillin and the broad-spectrum antibiotics. Local lesions are usually sterilized within 24 hours. However, an inflammatory factor elaborated by the anthrax organisms produces a typical pathological cycle. Anthrax meningitis is the most serious complication of cutaneous anthrax. Spread of anthrax from person-to-person is practically unknown.

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DR. WILBAR: Those of us who are public health minded will probably have to suspect that the plant manager had a prophylactic injection of penicillin

before he rubbed the material on himself.

The next paper will be given by Dr. Milton Werrin, Chief, Public Health Veterinary Medicine Section, Department of Public Health, City of Philadelphia. The paper will be on "Attempt at Preventing Cutaneous Anthrax by Use of a Protective Lotion". Dr. Werrin.

ATTEMPT AT PREVENTING CUTANEOUS ANTHRAX BY USE OF PROTECTIVE LOTION

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Protective lotions and ointements have been used in industry for many years, primarily in the chemical industries under varied conditions and against numerous irritants. While protective lotions are low on the list of preventive measures they are often the only available means of protection. In factories processing raw wool, hair, and leather, the problem has not been the protection of the worker against chemical irritants but rather the protection of the skin against the entrance of the anthrax organism, and more specifically against the spore of this organism.

A study of the epidemiological record of 72 cases that occurred in Philadelphia during the last seven years showed that approximately 97% of the anthrax cases occurred after exposure of the skin. The areas of the body most frequently involved were the hands and forearm, face, and neck. Most of the work performed in a wool, hair, and hide processing plant precludes the use of protective clothing; the face and neck being particularly vulnerable.

A further analysis of these data showed that most of the cases have occurred among those employees working in the spinning department of hair processing establishments. In this operation the use of gloves to protect hands and arms is impossible, since the operation must be performed with bare hands; even sleeves cannot be used by the workers for protection because of the rapidly revolving machinery in which they could easily become entangled. Many workers have a dislike for the use of protective clothing, claiming that it interferes with

easy movement and that it is uncomfortable in warm weather.

So far as the author has been able to determine from the literature, this report describes the first effort to prevent cutaneous anthrax by means of a protective lotion. The lotion was not selected for the purpose of destroying the anthrax organism on the skin; the lotion was used primarily to set up a protective barrier against the organism, especially to cover minute tears and abrasions of the skin following shaving, scratching, and contact with rapidly moving machinery. Indirectly, one of the reasons for the use of the lotion was that it was thought that it would reduce the inadvertent scratching and itching experienced by the workers employed in a dusty, hair-or wool-laden atmosphere. Many authors are of the opinion that scratching by the workers is the principal method of introducing the organism into the pores and layers of the skin.

Besides the protective barrier aspect of the lotion, it had also to be safe and of low-sensitizing action. It had to be bland and neutral, or slightly acid, to correspond to the chemical reaction of the skin itself. It could not interfere with normal action of the skin glands and had to be easily removed with mild soap and warm water.

The type of lotion obtained was able to satisfy the above requirements. It consisted of a light vanishing cream base into which was incorporated a water soluble shellac. When applied to the face, neck, arms, and hands it disappeared quickly, leaving a shiny film over the skin. There was a slight but definite loss of feeling on those areas covered by the lotion. During the entire period in which this product was used, not one case of skin sensitization occurred. A few workers claimed that the skin became dry following its use. A majority of the employees stated that the skin felt refreshed and cleaner after the product was removed by washing.

In order to establish whether or not the lotion would protect against the anthrax organism, one plant was selected to carry on this experiment. This plant employed 220 persons and had a rather constant employment rate with a slight decrease of employment during the summer months. During the last seven years, 20 cases of cutaneous anthrax occurred in the plant. Eleven of the infected persons were spinners and the rest were employed in the picker, carding, and drawing departments. One case involved a metal polisher.

The owners were cooperative and gave the writer every help and consideration. Before the lotion was used, an educational campaign was started. Material which would furnish each employee the answer to questions concerning the lotion was distributed. Posters urging the use of the product were hung in the dressing rooms. Employees were contacted in small groups and given a brief lecture on the use of the lotion.

The experiment was started two weeks after a case of anthrax had occurred. The workers were very receptive; it is believed because of this particular case. On February 22 the product was placed in each wash room and the employees started its use. The instructions asked the workers to apply the product as soon as they reported for work. Before going to lunch, the face, neck, and arms were washed. Upon returning from lunch, the lotion was reapplied and not removed until the end of the day's work.

Since the above date and up to the present (October 1, 1954), three cases of anthrax have occurred in the establishment. All cases involved spinners.

A brief summary of each case is as follows:

Case 1: A spinner contracted the infection after removing a splinter of hair from the fleshy part of the thumb. The needle was not sterilized and no dressing or antiseptic was used to cleanse the wound.

Case 2: A worker received an infection of the hand after bruising it on a piece of machinery. No medication or dressing was applied to the area.

Case 3: A worker received a lesion about the area of the temple. No scratch or cut was present before the lesion occurred and the patient claimed that she used lotion faithfully but became infected anyway.

The last case is the only one in which it may be claimed that the lotion failed to protect. The question as to whether these products can provide a measure of protection for workers in the wool, hair, and tanning industries is still left unanswered. It would seem that the use of such products could be of some benefit in prevention. Two of the three observed cases occurred following severe bruising and splinter embedment, and no lotion or ointment could be expected to prevent the entrance of the anthrax organism under these circumstances.

However, observation of the employees over many months, disclosed instances when the product was not used or was used reluctantly. Following a case of anthrax, there would be a sudden increase in the use of the product. This diligent use of the lotion would last for a few weeks and then there would be a decrease in its use until the next case of anthrax arose.

The lotion is still being employed at the above plant in spite of the fact that practically the same number of cases have occurred this year as in 1953, when four cases were reported. The author is of the opinion that a more basic type of prevention should be employed, such as sterilization of the raw material before it reaches the workers; or, if this is not feasible, the use of a safe and approved vaccine on each employee in these plants.

The reason for this conclusion is that the application of a lotion or ointment is personal and elective. It depends on the individual inclination of each worker, as supervision of the employees twice daily is difficult

There may be some plants in other sections of the country where the incidence of the disease has been noted recently, and the workers are fearful of their safety. In such a plant, there would probably be more cooperation and greater use of the product. An experiment held under these circumstances might produce more concrete results. In Philadelphia the average worker has little fear of anthrax and thus is reluctant to apply the lotion routinely.

Summary

1. A protective lotion was applied to the hands, arms, face, and neck by approximately 220 employees of a hair processing establishment for a period of more than eight months.

2. Three cases of cutaneous anthrax were reported during this period; two of these cases were reported following hair embedment and severe bruising of the skin; in one case it was judged that the lotion failed to protect.

3. Theoretically, the use of protective lotion appears to have some merit, but its application by the workers is difficult to supervise.

4. It is the writer's belief that a more basic method of prevention is needed, one that is not elective and does not depend on employee cooperation.

DR. WILBAR: Now Dr. A. G. Wedum, Chief, Biological Safety Division, Camp Detrick, Frederick, Maryland, will report to us on "Active Immunization with a Soluble Antigen from Cultures of Bacillus Anthracis". Dr. Wedum.

ACTIVE IMMUNIZATION WITH A SOLUBLE ANTIGEN FROM CULTURES OF BACILLUS ANTHRACIS

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Although a measure of success in immunization against anthrax was one of the early accomplishments of the science of immunology, advances in the theory and practice of immunization against this infection during the fifty years following this initial success may be reviewed very briefly. Bail in 1904 (1), showed that the antigen responsible for development of immunity to infection was present in the edema fluid of anthrax lesions, and these observations were confirmed and extended somewhat by subsequent workers. The protective antigen remained uncharacterized, however, and attempts to produce it apart from the animal body were unsuccessful until the classical studies of Gladstone, published in 1946 (2). This investigator demonstrated that protective antigen was elaborated during growth of the organism in whole serum under rather critical conditions. The antigen was present in the filtrate of the culture and not in the bacterial cells. Heckly and Goldwasser, working at Camp Detrick, confirmed these observations and demonstrated elaboration of protective antigen in a medium composed of blood ultrafiltrate and serum albumin (3).

Procedures for immunization with living spore vaccine were advanced considerably by the work of Sterne in South Africa (4). This investigator used a non-encapsulated avirulent mutant for immunization of animals and the vaccine has proved safe and effective in the field. Although this procedure was a distinct improvement over older spore vaccines and it has found increasing application in veterinary medicine, it seemed apparent that an effective sterile antigen would have definite advantages, especially for immunization of man.

The present program of investigation has been directed toward development of procedures for production of such an antigen. It is proposed to summarize briefly some of the results of these studies. Numbers of our colleagues have contributed greatly to these investigations, particularly Dr Virginia McCann, Mr. Milton Puziss, Dr. Thomas Green, Miss Winifred Jones, Mrs. Mary Hedberg, Mrs. Janet Slein, and Mr. Ralph Kanode.

Development of the chemically-defined medium for elaboration of the protective antigen was the result of a process of gradual substitution in complex media. It should be pointed out that the only established property of the protective antigen is its ability to immunize animals so that they survive a challenge that is fatal for normal animals. In all of the present studies, therefore, antigen activity was detected or estimated by immunization and challenge of rabbits or guinea pigs. This burdensome and rather inaccurate assay procedure has limited the scope of the experiments and has made it necessary to leave numerous aspects of the field uninvestigated. It is hoped that further study will reveal other immunological or biochemical properties of the antigen and thus lead to a simpler and more quantitative assay procedure.

The development and simplification of media and cultural conditions for antigen production have been described in some detail in recent publications (5, 6, 7) so that only a brief summary of the findings needs be presented here. The elaboration of antigen in a medium composed of serum albumin and blood ultrafiltrate (3) was confirmed and it was found possible to substitute a modification of the chemically-defined medium of Brewer et al. (8) for the blood ultrafiltrate. This modified medium, enriched with 1% crude bovine serum albumin, supported satisfactory elaboration of antigen.

Gladstone (2) had suggested that one of the limiting factors for accumula-

tion of protective antigen in cultures was the activity of the anthrax protease. It was suggested that this enzyme was elaborated during growth and that it destroyed the protective antigen if growth of the culture was allowed to continue to a maximum. At this stage of the program, accordingly, non-proteolytic mutants of B. anthracis were isolated (9) and one of them was used subsequently as inoculum for elaboration of antigen.

Antigen was not elaborated when crystalline bovine albumin was substituted for crude albumin as enrichment for the chemically-defined medium mentioned previously. Several substances, that might contaminate the crude albumin, were investigated and it was determined that addition of 0.0001 percent bilirubin to the crystalline albumin medium allowed elaboration of antigen equivalent to that obtained with crude albumin. After sintered glass filters were substituted for the Seitz filters, which had been used up to this point, it was noted that the albumin could be omitted and the first indications of elaboration of antigen in protein-free media were obtained.

Further modifications in the composition of the medium and recognition of the instability of the antigen in the fluid state then allowed elimination of the bilirubin. Experimental support for a satisfactory explanation of this rather tenuous series of observations has not been attempted because of the laborious assay procedure for the antigen.

Thus a medium containing only substances of known and relatively simple structure was developed and the influence of each constituent on elaboration of antigen was then studied (6). It was determined that glycine, alanine, lysine, cystine, glutamine, uracil, and adenine could be omitted from the medium individually or in combination and that the concentrations of theonine and proline could be reduced considerably. The latter observation was of importance in

reducing the cost of the consituents of the medium to approximately $0.30 per liter. Sodium bicarbonate, calcium ion, leucine, isoleucine, methionine, proline, phenylalanine, and histidine were necessary for elaboration of antigen, although they were not essential for growth. It is of interest that Thorne et al. (10) have demonstrated that isoleucine and phenylalanine are also essential for elaboration of the capsular polypeptide of B. anthracis. The composition of 599 medium, which was used for production of antigen in most subsequent work, is given in Table I

TABLE I

Composition of 599 Medium

Constituent	Molar Concentration	Constituent	Molar Concentration
dl-Serine	0.0002	dl-Phenylalanine	0.0004
dl-Threonine	0.0005	l-Tryptophan	0.00025
dl-Valine	0.0005	Calcium Chloride	0.0001
dl-Leucine	0.001	Magnesium sulfate	0.00004
dl-Isoleucine	0.001	Manganous sulfate	0.000005
dl-Aspartic acid	0.0005	Ferrous sulfate	*0.0005
l-Glutamic acid	0.0011	Potassium dihydrogen phosphate	0.005
l-Arginine.HCl	0.0005	Dipotassium hydrogen phosphate	0.005
l-Histidine.HCl	0.0005	Sodium bicarbonate	*0.03
l-Cysteine.HCl	0.00005	Guanine.HCl	0.000014
dl-Methionine	0.0002	Thiamin.HCl	0.0000003
l-Proline	0.00025	Glucose	*0.0056

* These constituents were sterilized separately and added aseptically to the autoclaved medium containing the other constituents. Ferrous sulfate solutions were sterilized by filtration; sodium bicarbonate and glucose solutions by autoclaving.

Sterile filtrates of cultures of non-proteolytic encapsulated or non-encapsulated strains in this medium contained the protective antigen. The antigenic activity could be concentrated and stabilized by lyophilization. This procedure has been used for studies on elaboration of antigen. For practical pur-

poses, however, precipitation with alum was found to be satisfactory for concentration and stabilization of the antigen. Potassium aluminum sulfate was added to the filtrate to a concentration of 0.1 percent and the pH was adjusted to 5.9 with dilute hydrochloric acid. The precipitate settled rapidly and was washed with 0.9 percent sodium chloride solution (saline). The precipitate was then resuspended in saline at 1/10 in initial volume of the filtrate and 1-10,000 merthiolate was added. This constitutes the stock antigen

Representative results of the assay of the alum-precipitated antigen in rabbits are summarized in Table II. The animals were immunized by intracutaneous injection of five 0.5 ml doses of dilutions of the stock antigen on alternate days. The challenge dose of 10,000 spores, representing approximately 100 LD_{50}, was given 7 days after the last injection of antigen. This immunization procedure was carried over from our earlier work and was used for consistency; satisfactory immunity may be produced in rabbits by a less extensive course of immunization.

TABLE II

Immunization of rabbits with alum-precipitated antigen

Total amount of stock antigen per animal*	Challenge dose	No. surviving / No. challenged
0.25 ml	10,000 spores	18/20
0.1 ml	10,000 "	16/21
0.03 ml	10,000 "	12/15
none	10,000 "	0/19

* Given in 5 injections on alternate days; 1st, 3rd, 5th, 7th, and 9th days.

Subcutaneous challenge 1 week after immunization was made with the equivalent of 100 M.L.D.

Results on the duration of the immunity produced in monkeys are summarized in Table

in Table III. The animals were immunized with a total of 1.5 ml of stock antigen in two doses, two weeks apart. At various intervals thereafter, groups of three animals were challenged by intracutaneous injection of 50,000 to 100,000 spores. It may be noted that effective immunity persisted for a year or more. Satisfactory immunity to respiratory challenge was also induced in monkeys by similar immunization, as shown by the results presented in Table IV.

TABLE III

Duration of immunity to intracutaneous challenge in monkeys with 50,000 to 100,000 spores.

Interval between immunization* and challenge	No. surviving / No. challenged
2 weeks	3/3
16 weeks	2/3
30 weeks	3/3
58 weeks	3/3
normal controls	0/4

* 1.5 ml stock antigen per animal in 2 doses, 2 weeks apart.

TABLE IV

Immunity to respiratory challenge in monkeys

Animals	Average challenge dose	No. surviving / No. challenged
immunized	60,000 spores	3/4
control	60,000 "	0/4
immunized	1,500,000 "	4/4
control	1,500,000 "	0/2

Animals immunized by 2 doses of vaccine given 2 weeks apart.

No primary toxicity of fluid or alum-precipitated preparations of antigen could be demonstrated in mice or guinea pigs. The material was well tolerated by rabbits and monkeys during the immunization experiments. Careful gross and microscopic examinations revealed no specific lesions in animals

that had received the antigen. Accordingly, immunization of man with the alum-precipitated antigen was initiated, beginning with small numbers of volunteers.

Results have been reported (7) on the results of 1,936 injections into 660 persons. Three subcutaneous injections of 0.5 ml were given at intervals of 2 weeks. A similar booster injection was given after 6 months. The antigen was well tolerated. The incidence of mild systemic reactions was 0.7 percent. These reactions consisted of mild, generalized aching, slight headache, and mild to moderate malaise of 1 to 2 days duration. The more severe febrile reactions that are rather common following administration of diphtheria, typhoid, plague, and rickettsial vaccines were not encountered.

Characteristic local reactions were noted in a small proportion of cases. These consisted of painless, brawny swellings 5 to 10 cm in diameter, which appeared 12 to 18 hours after the injection. The reaction reached its maximum extent on the second day, when the upper arm was significantly enlarged. In some cases the swelling extended to the mid-forearm. Local itching was a frequent complaint; this was relieved by antihistaminic drugs. The swelling began to decrease between two and three days after the injection and disappeared completely by the fifth day. The incidence of local reactions is summarized in Table V. It may be noted that no reactions occurred after the first injection and that the incidence increased with the number of previous injections. This suggests that the phenomenon has an allergic basis.

TABLE V

Local reactions during immunization of man with alum-precipitated protective antigen

Injection	Persons injected	% local reactions
1st	660	0.
2nd	650	0.6
3rd	537	2.2
booster	445	2.6

Our observations on elaboration of antigen in non-protein medium have been confirmed in England by Belton and Strange (11), who developed a case in hydrolysate-yeast extract medium for elaboration of antigen. The cost of the chemically-defined medium is relatively low, however, and we have not considered it desirable to utilize media containing natural products of variable composition. Additional confirmation of the present work has been obtained by Dr. Henry Devlin and his associates at Parke, Davis, and Company, under a Camp Detrick research contract. These workers have successfully produced the alum-precipitated antigen under conditions suitable for large-scale production.

Studies of the elaboration and properties of the antigen are being continued. In vew of the general effectiveness of the antigen in producing protective immunity in laboratory animals, it would be surprising if the antigen did nct immunize large animals and man. However, direct investigation will be necessary to determine whether significant immunity is in fact produced and whether its degree and duration is sufficient to establish the antigen as a practical product for use in the field. We are unable as yet to explain the mode of action of the antigen or to interpret its crucial role in the host-parasite relationship in anthrax. It is our hope that investigations in progress will provide solutions to certain of these problems, and that the investigations may be of general inter-

est in the field of infection and resistance.

Summary

A sterile, alum-precipitated anthrax antigen has been produced. The product is free of foreign protein, and it induced effective immunity in rabbits, guinea pigs, and monkeys. Significant immunity persisted for more than three months in rabbits and for more than 14 months in monkeys. Immunity in monkeys was effective against both intracutaneous and respiratory challenge. The product was devoid of toxicity when tested in mice, guinea pigs, rabbits, and monkeys. Injection of the antigen into man was well tolerated. No serious reactions were encountered and moderate local reactions were infrequent.

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DR. WILBAR: Now we will hear from Dr. Herman Gold of Chester, Pennsylvania, on "Present Day Treatment of Anthrax". Dr. Gold.

THE TREATMENT OF ANTHRAX

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In reviewing the records of our cases of cutaneous anthrax, we were struck by the successive changes in the therapeutics of this disease, changes that reflect the development of modern antibiotics. The story of anthrax mirrors that of pneumococcic pneumonia. From 1933 to 1939 we treated 21 cases of cutaneous anthrax with specific anti-anthrax serum. During this interval our efforts were concentrated on finding the optimum dose and the most effective route of administration of the serum. Although the results obtained following the intravenous injection of 500 to 1000 cc of serum were very satisfactory as far as the mortality rate was concerned, the morbidity figures left much to be desired. The disadvantages and complications that followed the intravenous injection of large doses of the rather crude horse serum are too well known to require elaboration.

It was with great anticipation that in 1939 we turned our attention to the sulfonamides and found them to be effective in the treatment of human anthrax. In 1942 cases treated with the sulfonamides. At that time, sulfathizaole was considered to be the drug of choice. An initial dose of 2-3 gms followed by 1 gm every 4 hours for 2-3 days served to control the spread of the anthrax edema and brought about the disappearance of fever and other signs of systemic toxicity. Thereafter, chemotherapy was continued at a lower dose level until the edema and erythema cleared completely.

Under this treatment, an occasional failure was encountered. In such circumstances we resorted to anti-anthrax serum. Naturally, reactions to the sulfa drugs, such as hematuria and dermatitis, were encountered rather

often, but the advantages of chemotherapy as compared to the serum were so great that the serum was seldom used.

From 1942 to July of 1947 we treated 14 additional cases of anthrax; 12 with sulfathiazole and 2 with sulfamerazine. These patients were treated in ambulatory fashion unless the home situation or the patient's attitude warranted hospitalization. Our experience with this group of patients confirmed the previously published findings (1). Eleven of the patients were cured by the sulfonamides. One case (#76, Table 3) with anthrax of the forearm received 3 gms of sulfathiazole followed by 1 gm every 4 hours for 3 days, but the edema kept spreading and lymphangitis appeared on the upper arm. He was then given an injection of 100,000 units of crystalline penicillin followed by 40,000 units every 3 hours with control of the infection within 24 hours.

Thereafter we used penicillin and the various broad-spectrum antibiotics in the treatment of anthrax. Before summarizing our clinical experience with these therapeutic agents, we would like to report the results of in vitro sensitization tests performed on cultures of anthrax bacilli isolated from some of our patients (Tables 1 and 2).

It would appear from these tests, performed in the Hospital of the University of Pennsylvania, that the anthrax bacillus is sensitive to terramycin, erythromycin, aureomycin, achromycin, chloromycetin, penicillin, and streptomycin and is resistant to neomycin and polymyin.

PENICILLIN: - Penicillin, either crystalline or in repository form, was used in 5 patients. The pertinent data is summarized in Table 3.

In general, we prefer to use a large initial dose of crystalline penicillin (100,000 - 500,000 units) followed by either 20-25,000 units every 3-4 hours or preferably 600,000 units of procaine penicillin in suspension every 12 to 24 hours

depending on the severity of the infection. This is continued for a day or two or until the spread of the edema is checked and the local erythema, if present, subsides. Once the latter is achieved, the procaine penicillin dosage is reduced (300,000-600,000 units daily), and treatment is continued until the edema clears entirely. This usually occurs in 24 to 48 hours. In our cases, the total dosage of penicillin ranged from 980,000 to 6,000,000 units given in from 2 to 7 days, respectively. We, as well as others (2), have observed some patients who showed a temporary increase in the erythema and swelling around the lesion in the first 24 to 36 hours of penicillin treatment. Painless adenopathy may persist for days or weeks after the patient is otherwise well; it is no indication for further therapy. The "pustule" itself undergoes the usual changes of vesiculation, eschar formation and separation, and final epitheliazation regardless of treatment given and appears to be unaffected by it; however, in most patients under penicillin treatment, anthrax bacilli disappeared from the lesion rather promptly (24-48 hours). In one case (#101) we recovered the organism as late as 60 hours after treatment had been started and the patient had received a total of 3,300,000 units of penicillin in oil.

The disadvantages of penicillin therapy are not great or serious: (1) Injections, as such, are sometimes objectionable to the patient; (2) If crystalline penicillin is used, the multiple injections require hospitalization; (3) Sensitization reactions do occur and although usually not serious they increase the morbidity and the duration and cost of illness.

AUREOMYCIN: We have treated 6 cases of anthrax with aureomycin given by mouth with excellent results (Table 4). After a somewhat larger initial dose, 500-750 mg of aureomycin were given every 4 to 6 hours for the first day or two, or until the edema receded; thereafter, the dose was decreased

to 250-500 mg and/or the interval between doses was lengthened until the edema and erythema cleared, the pain and tenderness over the regional lymph nodes had subsided, and the fever and malaise had cleared. The total dose of aureomycin ranged from 4.5 gms given in 54 hours to 20.5 gms in 8 days. As with penicillin, a temporary increase in the edema was noted during the first day of treatment with aureomycin. Positive smears and cultures were obtained in these patients during a somewhat longer interval of time (up to 5 days) than in the penicillin-treated cases. This was also true for the other broad-spectrum antibiotics.

The advantages of oral therapy which is not associated with sensitization phenomena are obvious; however, the severe nausea and vomiting induced by aureomycin in some patients was a trouble-some and objectionable feature.

CHLOROMYCETIN: Seven patients were treated with chloromycetin (Table 5). One of them (#92) had been placed on adequate doses of terramycin which had failed to control the infection at the end of 36 hours. Most of the cases received an initial dose of 1 gm, followed by 0.75 gm every 4 hours until the edema subsided; then the interval was lengthened and the dose was reduced gradually. The smallest total dose given was 2.25 gms in 2 days, and the largest was 24.75 gms in 7 days. In all cases, the edema was brought under control in 24-48 hours after treatment was started. As was observed in many cases treated by other means, case #94 displayed a palpable non-tender preauricular node two weeks after treatment had been stopped and one week after the ulcer had healed.

Chloromycetin was well tolerated; no untoward reactions were noted. However, we have stopped using this drug because of its reported depressive effects on the hemopoietic system.

TERRAMYCIN: Fifteen patients were treated with this drug; in 14, the results were excellent (Table 6). The failure has been referred to under chloromycetin. 500-750 mgs of terramycin were given every 4-6 hours depending on the severity of the case, and until the edema was brought under control, usually in 24 to 48 hours. The dosage was then decreased. The total dose given ranged from 3.0 gms in 3 days (#106 - anthrax of leg) to 29.5 gms in 8 days (#95 - anthrax of the forearm).

No untoward reactions were seen and the drug was well tolerated.

ACHROMYCIN: Six patients were treated with this new antibiotic with excellent results in all (Table 7). One case (#111) with a "pustule" on the left upper lid, was initially treated with large doses of penicillin (4,000,000 units daily) because of the location of the lesion, its severity, and our anxiety to obtain the earliest possible control of the infection in order to secure a good cosmetic end-result. As soon as the edema began to recede, this patient was discharged from the hospital and was placed on achromycin with excellent results. The average dose was 500 mgs every 4-6 hours; the total dose ranged from 10 gms in 5.5 days to 14 gms in 8 days.

The drug was well tolerated and no untoward reactions were recorded.

Two cases were successfully treated with erythromycin, 200 mgs every 4 hours for 2-3 days checked the spreading edema. We have never used streptomycin because of the potential hazards inherent in its use (8th nerve damage).

The treatment given to our cases was highly individualized and the dosage used was arbitrary; perhaps much smaller doses of the antibiotics would suffice. However, we felt it advisable to err on the side of conservatism and we aimed to achieve in the human patient a blood level of a given antibiotic several times

its effective in vitro concentration. Titrations were carried out in some patients and the values obtained are shown in Table 8

It is clear that the therapeutic management of anthrax is a systemic one; locally we place the affected part at rest, if possible; we cover the lesion with a sterile dressing, making sure that no one but the medical attendant removes it. We have used local applications of aureomycin and terramycin ointments, and have tried to digest the eschar with streptokinase, but the results were at best inconclusive. Prompt chemical treatment of the wound with tincture of iodine and/or phenol did not prevent the development of anthrax.

To complete the picture, we must refer to two questions:

1. Is treatment of anthrax necessary? 2. Do antibiotics prevent the disease if given soon after injury, during its incubation period? As to the first, we have had one patient with anthrax of the arm who displayed little edema and no adenopathy and who recovered when given sodium bicarbonate tablets as a placebo. He was carefully watched, and our clinical impression that he would not require any specific treatment proved to be correct. But we would not recommend this as a general procedure. The very first case of anthrax that we saw in 1933 died, and the mortality figures collected in this country verify the dangerous character of this infection. From 1919 to 1923, the death percentage rate in the U.S.A. was 23 plus; from 1924 to 1928, 20 plus; from 1929 to 1933, 22 plus; and from 1934 to 1938, 16 plus (3). Since the advent of penicillin, large series of anthrax cases have been reported from various centers (2, 4, 5), in addition to our own (6), without a single death.

As to the second question; - we do not profess to know a definitive answer. We have seen a patient with a laceration of the thumb from which we recovered anthrax bacilli; he was given terramycin 0.5 gm every 4 hours and failed to

develop any clinically recognizable anthrax lesion. On the other hand, we had a patient (case #100) who was severely injured with a multiple compound fracture of the forearm and deep third degree burns of the entire extensor surface of the right forearm. He was given very large doses of penicillin daily, immediately following the injury, and yet on the fifth day developed the most extensive anthrax lesion that we have seen. The escar covered the extensor surface of the forearm from the netacarpo-phalangeal joints to just below the elbow. I think it was probably the largest single lesion recorded in medical literature. He recovered after further treatment with penicillin, terramycin, and chloromycetin.

From these considerations, it is clear that the modern antibiotic treatment of anthrax is of value and should be instituted as soon as possible after the diagnosis is established bacteriologically. In this respect, I wish to state that all of our 114 cases were clinically suspected and proved by smear and culture to be anthrax.

CONCLUSIONS

1. Our personal experience with 56 cases of anthrax treated since 1942 is reviewed; no deaths were encountered.

2. Comparison with our previously reported study of 60 cases of anthrax shows that the antibiotics offer the best means of securing a cure with the least morbidity and disability.

3. The broad-spectrum antibiotics make it possible to treat these patients in ambulatory fashion; this, plus the shortened duration of the anthrax infection, make them highly desirable therapeutic agents.

4. In our experience terramycin, achromycin, and erythromycin appear to be the drugs of choice.

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TABLE 1. -- BACTERIAL SENSITIVITY TESTS**

CASE NO.	AUREOMYCIN MICROGRAM	CHLOROMYCETIN MICROGRAM	PENICILLIN MICROGRAM	STREPTOMYCIN MICROGRAM	NEOMYCIN MICROGRAM	POLYMYXIN MICROGRAM	TERRAMYCIN MICROGRAM
84	pi0.1 * ci1.0	3.12	<0.1	3.12	5.0	>25.0	<0.1
85	pi0.1 ci1.0	3.12	pi0.1 ci1.0	pi 3.12 ci12.50	5.0	>25.0	<0.1
86	pi0.1 ci1.0	3.12	<0.1	pi 3.12 ci12.50	5.0	>25.0	<0.1
87	pi0.1 ci1.0	3.12	pi0.1 ci1.0	pi 3.12 ci12.50	5.0	>25.0	<0.1
88	<0.1	12.50	pi1.0 ci5.0	pi 3.12 ci12.50	pi 5.0 ci25.0	>25.0	<0.1
89	<0.1	pi 3.12 ci12.50	pi1.0 ci5.0	pi 3.12 ci12.50	pi 5.0 ci25.0	>25.0	<0.1
90	<0.1	pi 3.12 ci12.50	<0.1	pi 3.12 ci12.50	5.0	>25.0	<0.1
91	<0.1	pi 3.12 ci12.50	pi0.1 ci1.0	3.12	5.0	>25.0	<0.1
92	<0.1	3.12	1.0	3.12	5.0	>25.0	<0.1
93	<0.1	pi 3.12 ci12.50	<0.1	pi 3.12 ci12.50			<0.1
94	<0.1	pi 3.12 ci12.50	<0.1	pi 3.12 ci12.50			<0.1

* pi = partiol inhibition, ci = complete inhibition.

** Performed in the Laboratory of the Division of Infectious Diseases of the Hospital of the University of Pennsylvonio through the courtesy of Dr. W. P. Boger

TABLE 2 -- BACTERIAL SENSITIVITY TESTS**

CASE NO.	AUREOMYCIN 4 mcg/ml	CHLOROMYCETIN 15 mcg/ml	PENICILLIN 1 unit/ml	STREPTOMYCIN 15 mcg/ml	TERRAMYCIN 6 mcg/ml	TETRACYCLINE 5 mcg/ml	SERIAL DILUTIONS Erythromycin	SERIAL DILUTIONS Tetrocycline
110	Sensitive	Sensitive	Sensitive	Sensitive	Sensitive	- - - -	0.19 mcg/ml	0.048 mcg/ml
111	Sensitive	Sensitive	Sensitive	Sensitive	Sensitive	- - - -	0.09 mcg/ml	12.5 mcg/ml
113	Sensitive	Sensitive	Sensitive	Sensitive	Sensitive	Sensitive	- - - -	- - - -

**Performed in the Laboratory of the Division of Infectious Diseoses of the Hospital of the University of Pennsylvonio through the courtest of Dr. E. L. Foltz.

TABLE 3

PENICILLIN

CASE NO.	AGE	C	S	DEPT.	SITE	ONSET	FIRST SEEN	FIRST TREAT	DRUG	DOSAGE	REMARKS
76	54	W	M	Carder	Fore-arm	7-11-47	7-11	7-11	Sulfathiozole	3 Gm.- 1 Gm./4 h. T.D: 21.5 Gm./2.5 days	Edema & lymphangitis of arm increased by 3rd day of Sulfa treatment.
									Crystalline Penicillin G.	100,000 U.; 40,000 U./3 h. x 6; /4 h. x 8; 20,000 U./4 h. x 16 T.D: 980,000 U./4.5 days	Treatment changed to Penicillin; improvement in 24 hr. Returned to work: 8-11-47
78	44	W	M	Carder	Fore-head	2-15-48	2-18	2-18	Crystalline Penicillin G.	500,000 U.; 50,000 U. /3 h. x 5; 200,000 U., /3 h. x 2; 50,000 U./4 h. x 17 T.D: 2,000,000 U./3.5 days	In 24 hrs., adenopathy was smaller but periorbital edema increased; latter subsided by 3rd day. Returned, to work: 3-7-48
79	36	C	F	Finisher	Chin	3-21-48	3-24	3-24	Penicillin in oil	3-24; 1,500,000 U. 3-25; 900,000 U.; 600,000 U. daily x 2; 300,000 U. T.D: 3,900,000 U./5 days	Improvement noted on 3rd day; 4-3 eschar off; 4-11 submental node, size of marble; 4-20 ulcer healed but node still palpable. Returned to work: 4-12-48
80	34	W	F	Spinner	Wrist	11-1-48	11- 4	11- 4	Penicillin in oil	600,000 U. daily x 2 T.D: 1,200,000 U./2 days	At end of 48 hrs., pt. toxic, T = 100.6°. Edema and erythema spreading into arm and axillary fold.
									Crystalline Penicillin G.	500,000 U.; 500,000 U. in 2 doses /4 h. 50,000 U./4 h. x 16; 20,000 U./4 h. x 6 T.D: 1,920,000 U./4 days	Placed on crystalline penicillin. Improved on 2nd day of therapy when culture wos negative for anthrax. Returned to work: 11-22-48
101	20	C	M	Carder	Lip	3-31-52	4-1	4-1	Penicillin in oil	1,200,000 U. daily x 2; 4-3: 900,000 U.; 4-4: 600,000 U.; 4-5: 900,000 U.; 4-6: 600,000 U.; 300,000 U. x 2 T.D: 6,000,000 U./7 days	Smear & culture taken 60 hrs. after treatment (3,300,000 U.) positive. Swelling less on 3rd day, but tender cervical node present. Local streptokinase ? value. Culture neg. on 6th day. 4-17-52: lesion healed; cervical node still visible. Returned to work: 4-15-52

TABLE 4

CHLORTETRACYCLINE H Cl. (AUREOMYCIN)

CASE NO.	AGE	C	S	DEPT.	SITE	ONSET	FIRST SEEN	FIRST TREAT	DOSAGE	REMARKS
77	52	W	M	Carder	Wrist	1-11-49	1-13	1-18	750 mg./4 h. for 3 days. 500 mg./4 h. x 3, then /6 h. T.D: 19.75 Gm./6 days	Edema subsided in 48 hrs. but culture pos. for anthrax. Organism very sensitive to aureo (I-9.25 mcg/cc.) resistant to penicillin (I-30 U./cc.) On 3rd day adenopathy cleared; smear & culture neg. on 4th day. Returned to work: 1-31-49
81	27	W	F	Spinner	Thumb	4- 8-49	4-9	4-10	750 mg./4 h. for 1 day; 500 mg./4 h. for 2 days; 250 mg./6 h. T.D: 11.25 Gm./4 days	Severe nausea and vomiting; local swelling subsided in 36 hrs.; culture pos. for anthrax 48 hrs. sensitive to aureo. (I-9.25 mcg/cc.); penicillin (I- 1 U./cc., Returned to work: 4-25-49
82	45	W	F	Drawer	Ear	7-29-49	8- 2	8- 3	500 mg/4 h. x 6; /6 hr. x 3 T.D: 4.5 Gm./2.25 days	Edema controlled in 24 hrs.; nausea and vomiting marked. Returned to work: 8-10-49
83	28	W	F	Drawer	Fore-arm	9-10-49	9-14	9-14	500 mg/4 h. for 3 days; 250 mg/4 h. x 5 T.D: 10.25 Gm./4 days	In first 36 hrs., increased edema and lymphangitis; subside subsided at end of 60 hrs. after treatment. Returned to work: 9-26-49
97	47	W	M	Machinist	Foot	7- 3-51 ?	7-10	7-10	1 Gm./6 h. x 8; 0.5 Gm./6 h. x 25. T.D: 20.5 Gm./8 days	Edema subsided in 24 hrs. On 4th day, smear pos. but culture neg. for anthrax. Inguinal adenopathy persisted for two weeks. Returned to work: 7-25-51
98	45	W	M	Drawer	Fore-arm	7-12-51	7-14	7-14	750 mg/4 h. x 13; 500 mg/4 h. x 16. T.D: 18 Gm./5 days	Edema subsided in 24 hrs.; smear & culture pos. for anthrax on 3rd day after treatment. Returned to work: 7-6-51

T.D. = Total Dose I. = Inhibition of growth

TABLE 5

CHLORAMPHENICOL H Cl. (CHLOROMYCETIN).

CASE NO.	AGE	C.	S.	DEPT.	SITE	ONSET	FIRST SEEN	FIRST TREAT	DOSAGE	REMARKS
84	41	W	F	Spinner	Fore-arm	11- 4-49	11-11	11-13	250 mg./6 h. T.D: 2.25 Gm. /2days	Treatment withheld until edema spread; controlled in 24 hrs. Smear and culture neg. for anthrax after 48 hrs. of treatment. Returned to work: 11-21-49
85	34	W	F	Spinner	Lip	4-14-50	4-18	4-18	1 Gm./6 h. for 3 days; 750 mg./6 h. x 2; 500 mg./6 h. T.D: 16 Gm./5 days	T. = 101.4°, subsided in 12 hrs.; edema spread for 1st 2 days, then subsided; smear and culture pos. for anthrax 42 hrs. after treatment (8 Gms.) and neg. on 4th day. Returned to work: 5-3-50
88	19	W	M	Spinner	Finger	5-30-50	6- 5	6- 5	1 Gm./6 h. for 3 days 500 mg./6 h. x 4 250 mg./6 h. T.D: 14.5 Gm./5 days	Edema less & pain in axillary node subsided in 18 hrs.; smear and culture pos. for anthrax 48 hrs. after treatment; neg. after 11 Gm. in 66 hrs. Returned to work: 6-12-50
89	36	W	M	Spinner	Neck	9-21-50	9-22	9-22	750 mg./4 h. for 4 days then gradually reduced to 500 mg./8 h. T.D: 23.75 Gm./6.5 days	Edema increased in first 24 hrs., then subsided; 9-25: smear pos. for anthrax; on 26th: smear & culture negative. Returned to work: 9-30-50
92	36	W	F	Doffer	Fore-arm	10-10-50	10-16	10-16	Terramycin: 500 mg./4 h. x 10 T.D: 5.0 Gm./2 days Chloramphenicol: 1 Gm; 750 mg./4 h. for 2 days; then /6 h. T.D: 21 Gm./6 days	First 48 hrs. increased toxicity, T: = 102°; spreading edema & cellulitis. Placed on chloromycetin with improvement in 24 hrs.; gradual subsidence of local signs over 4 days. Returned to work: 11-7-50
93	37	W	F	Spinner	Arm	10-31-50	11- 2	11- 2	1 Gm; 750 mg./4 h. for 2 days; 500 mg./6 h. T.D: 13.75 Gm./4.75 days	Edema subsided in 48 hrs.; smear and culture neg. for anthrax on 4th day of treatment. Returned to work: 11-13-50
94	18	W	F	Spinner	Cheek	11- 4-50	11- 6	11- 6	1 Gm.; 750 mg./4 h. for 4 days; 500 mg./6 h. T.D: 24.75 Gm./7 days	4½ mos. pregnant; edema af face increased in first 48 hrs., then subsided gradually; on 5th day af treatment, accas. anthrax B. seen on smear; glossitis an 7th day, responded to Vit. B; regianal node persisted 7 days after ulcer healed. Returned ta work: 11-15-50

TABLE 6

OXYTETRACYCLINE H Cl. (TERRAMYCIN).

CASE NO.	AGE	C.	S.	DEPT.	SITE	ONSET	FIRST SEEN	FIRST TREAT	DOSAGE	REMARKS
86	23	W	F	Spinner	Fore-arm	4-28-50	5-1	5-1	0.5 Gm./6 h. T.D: 6 Gm./3 days	Edema subsided in 2 days; 48 hrs. after treatment (4.5Gm.), occ. anthrax b. on smear but no growth on culture. Returned to work: 5-15-50
87	45	W	M	Spinner	Ear	5-9-50	5-12	5-10	Penicillin in oil: 300,000 U. daily x 3 T.D: 900,000 U./3 days Sulfadiazine: 1 Gm./4 h. T.D: 9.0 Gm./3 days	Spreading edema, erythema and painful regional adenopathy, notwithstanding treatment given by family physician from 5-10 to 5-12
									Terramycin: 750 mg./6 h. T.D: 15.25 Gm./6 days	Improvement in 36 hrs. after Terramycin Treatment. Smear and culture neg. for anthrax on 3rd day. Returned to work: 5-29-50
90	28	W	F	Spinner	Fore-head	10-11-50	10-13	10-14	500 mg./4 h. x 3 days then/8 h. T. D: 15 Gm./8 days	Treatment withheld till edema spread & regional node painful; local signs began to recede in 24 hrs. Smear & culture neg. for anthrax 48 hrs. after treatment. Returned to work: 10-31-50
91	36	W	M	Spinner	Cheek	10-11-50	10-12	10-12	750 mg./4 h. x 4 days then /6 h. T.D: 19.5 Gm./7 days	Edema increased in first 36 hrs., then receded; smear & culture neg. for anthrax on 5th day. Returned to work: 10-19-50
95	43	W	M	Spinner	Fore-arm	6-7-51	6-12	6-12	Penicillin in oil: 300,000 U. Terramycin: 1 Gm; 750 mg./4 h. for 5 days; 500 mg. /4 h. T.D: 29.5 Gm./8.5 days	Seen in Phila. Hosp. where penicillin was given. Edema & erythema subsided in 48 hrs. after terramycin. Returned to work: 6-25-51
96	36	W	F	Spinner	Wrist	6-25-51	6-28	6-28	500 mg./4 h. 7-2: 250 mg./6 h. T.D: 15 Gm./8 days	Edema increased in first 24 hrs; thereafter gradually less; 7-2: smear and culture neg. for anthrax. Returned to work: 7-19-51
99	26	W	M	Spinner	Neck	9-20-51	9-24	9-21	Penicillin in oil: 600,000 U. (9-21) 300,000 U. (9-22) T.D: 900,000 U./2 days Terramycin: 250 mg./4 h. (9-22)	Increasing toxicity and spreading edema while treated by family physician.
									750 mg./4 h. (9-24) 500 mg./6 h. (9-26) T.D: 13.75 Gm./4.5 days	After massive doses of terramycin, local signs controlled in 24 hrs. Returned to work: 10-12-51
102	34	W	F	Doffer	Finger	3-31-52	4-7	4-7	750 mg./4 h. x 2,500 mg./4 h. for 1 day then decreased to 250 mg./6 h. T.D: 7 Gm./3.5 days	Edema controlled in 24 hrs., but erythema overlying epitrochlear node persisted 48 hrs.; 4-10 Smear: 3 anthrax b. see; culture negative. Returned to work: 4-15-52
103	35	W	F	Drawer	Cheek	5-30-52	6-2	6-2	750 mg; 500 mg./4 h. T.D: 7.25 Gm./3 days	Edema of eye increased 1st day, then subsided. Returned to work: 6-10-51
104	32	W	M	Warehouse	Thumb	8-2-52	8-6	8-6	750 mg./4 h. x 2; 500 mg./4 h. x 6 then /6-8 h. T.D: 15.5 Gm./6 days	Edema less within 24 hrs.; epitrochlear and axillary nodes palpable for 12 days. Returned to work: 8-19-52
105	59	W	F	Spinner	Chin	8-16-52	8-18	8-18	500 mg./4 h. /2 days 500 mg./6 h. T.D: 9.5 Gm./4 days	Swelling increased first day, then subsided. Returned to work: 8-27-52
106	20	C	M	Carder	Leg	2-9-53	2-11	2-11	500 mg./6 h. T.D: 3.0 Gm./3 days	After 24 hrs.; pain lessened but inguinal node unchanged; no edema. 2-14 node smaller. Returned to work: 2-16-53
107	59	W	F	Burler	Fore-arm	2-25-53	2-27	2-27	500 mg./6 h. T.D: 14.5 Gm./7 days	Swelling, erythema & pain increased in first 3 days, then subsided. Returned to work: 3-9-53
108	32	W	M	Carder	Fore-head	3-9-53	3-11	3-11	750 mg./4 h. x 4, then 500 mg./4-6 h. T.D: 19 Gm./7 days	Edema increased in first 2 days, then subsided gradually. Returned to work: 3-23-53

TABLE 7

TETRACYCLINE H Cl. (ACHROMYCIN).

CASE NO.	AGE	C.	S.	DEPT.	SITE	ONSET	FIRST SEEN	FIRST TREAT	DOSAGE	REMARKS
109	59	W	F	Doffer	Thumb	2-3-54	2- 8	2- 9	500 mg./6 h.; 250 mg./6 h. (2-13) T.D: 10.5 Gm./6 days	2-11: Slight edema of thumb with some axillary tenderness but no adenopathy. Returned to work: 2-21-54
110	44	W	F	Spinner	Arm	2-24-54	2-26	2-26	500 mg./6 h. x 11; /8 h. x 9 T.D: 10 Gm./5.5 days	Swelling subsided in 48 hrs. Returned to work: 3-8-54
111	39	W	F	Spinner	Eyelid	2-28-54	3- 2	3- 2	Cryst. Penicillin G.: 1,000,000 U. Procaine Penicillin Susp: 1,000,000 U./12 hr. x 2;/6 h. x 12 T.D: 15,000,000 U-/4 days Achromycin (3-6): 500 mg./6 h. x 15; /8 h. x 13. T.D: 14 Gm./8 days	Smear and culture neg. for anthrax 18 hours after treatment. Edema definitely decreased but still present, with regional adenopathy when discharged from hospital and placed on Achromycin. Intraorbital edema and cervical nodes subsided gradually Returned to work: 3-17-54
112	48	W	F	Spinner	Nose	3-2-54	3- 6	3- 9	1 Gm; 500 mg./4 h. x 17; /6 hr. x 5 T.D: 12 Gm./4 days	Therapy delayed till edema, lymphangitis and adenopathy developed- local signs controlled in 48 hrs. 3-11: smear neg. for anthrax. Returned to work: 3-22-54
113	41	W	F	Spinner	Forearm	6-23-54	6-29	6-29	250 mg./6 h. x 12; /8 h. x 12. T.D: 6 Gm./7 days	Erythema and local edema increased in first 24 hours; controlled in 48 hours. Returned to work: 7-10-54.
114	32	W	F	Spinner	Thumb	8-3-54	8- 6	8- 7	500 mg./6 h. x 22; /8 h. x 3. T.D: 12.5 Gm./7 days.	Axillary adenopathy cleared in 48 hours. Returned to work: 8-17-54.

TABLE 8

CASE	DRUG	DOSE	PLASMA LEVELS, MICROGRAMS/ML. AFTER ORAL DOSE*					
			½ hour	1 hour	2 hours	3 hours	4 hours	6 hours
86	Terramycin	500 mg.	8	16	16	--	16	--
87	Terramycin	750 mg.	8	16	16	--	16	--
90	Terramycin	500 mg.	8	16	16	--	16	--
91	Terramycin	500 mg.	8	16	16	--	16	--
92	Terramycin	500 mg.	--	16	--	--	16	--
	Chloromycetin	750 mg.	--	120	120	90	60	--
84	Chloromycetin	250 mg.	--	--	<7.5	--	<7.5	<7.5
85	Chloromycetin	1,000 mg.	--	--	60	--	45	30
	Chloromycetin	500 mg.	--	--	20	--	10	5
88	Chloromycetin	500 mg.	--	20	20	10	20	--
89	Chloromycetin	750 mg.	--	20	15	7.5	15.0	--
93	Chloromycetin	750 mg.	--	22.6	30	22.6	--	--
94	Chloromycetin	750 mg.	--	22.6	30	15	15	--

* Performed in the Laboratory of the Division of Infectious Diseases of the Hospital of the University of Pennsylvania through the courtesy of Dr. W. P. Boger.

DR. WILBAR: The final paper of this symposium will be given by Dr. Joseph Shilen, Director of the Bureau of Industrial Hygiene, Department of Health of the State of Pennsylvania. He will talk on the Subject of "Medical and Educational Plant Programs". Dr. Shilen.

ANTHRAX -- MEDICAL AND EDUCATIONAL PLANT PROGRAMS

by
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The control of anthrax in industrial establishments handling and/or processing animal products such as skin, wool, and hair, may be secured by two methods: (1) by legislation, on the national level, prohibiting the importation of infected material into the country, or requiring sterilization of the material upon entry into our ports before it is shipped for industrial use; or (2) by the establishment of preventive programs in those plants which handle and process the infected material. The first method, which is the most desirable, is a matter of economic concern beyond the scope of a state industrial health agency. Naturally, the prohibition of infected material into the country would practically eliminate the hazard of exposure for employees in a plant. The use of the "Duckering" process in England has evidently resulted in the lowering of the morbidity rate of industrial anthrax there. However, as Wolff and others have pointed out, it is possible that, due to the English restrictions, a large amount of infected material has been diverted into the United States. I believe that Dr. Steele stated that during the period 1942-1950 when the Liverpool station was not operating a large amount of material was sent to the U.S. Since these methods involve matters of international policy and national policing, the Bureau of Industrial Hygiene in Pennsylvania has attempted the control of industrial anthrax at the plant level.

The ideal program for an industrial establishment to undertake for the prevention of anthrax would be for each plant to sterilize the infected material it receives. This, of course, would not protect such exposed workers as steve-

dores, truckers, and the like. Various attempts have been made to sterilize successfully infected material in the plants, but generally this has been on an experimental basis. Industry has been unwilling to accept steam sterilization of materials (wool and hair) because of possible damage to the physical properties of the material and the cost of integrating such methods into the process. Chemical methods of sterilization have been tried, and some show promise.

However, as Boyd and his associates have pointed out, any method to be used for industrial application must meet the following criteria: (a) the disinfectant or means should be completely effective; (b) it should be economical; (c) it should have effective action in the presence of organic matter without producing deleterious effects on animal products; (d) it should possess power of penetration; and (e) it should react at ordinary temperatures. Until a method is found which meets all the requirements of the industry and is effective in killing the anthrax spore, we believe that it would impose unnecessary hardship on the industry to ask them to accept a method which is still questionable or to demand that they experiment themselves.

Therefore, we attempt to maintain a program of prevention on the plant level, by employing known and approved methods of control which are applicable to all industrial hazards. The methods used are not compulsory but have been recommended to the plants as practical means of curtailing the incidence. Adherence to these recommendations vary according to the supervision exerted by the plant officials, but we have found that most plants comply with the majority of suggestions. Our control program may be divided into 3 categories: (1) medical; (2) environmental; and (3) personnel.

The medical control program calls for the employment of a plant physician, preferably on a full-time or part-time basis. But a large number of

plants may prefer to retain the physician on an "on call" basis. The physician should acquaint himself with all of the hazards present in the plant and have a knowledge of the methods of treatment for the specific illnesses which may occur. He should also be consulted on other phases of the protection program and should visit the plant periodically to ascertain their proper functioning. The installation and maintenance of adequate first aid facilities should be under his supervision, together with the training of first aid personnel. A registered nurse in charge of a dispensary is desirable. The responsibility for the indoctrination of the plant employees on the cause and nature of anthrax lies in the hands of the medical department. The use of pre-employment and periodic physical examinations is of paramount importance, for persons in poor health are susceptible to any infection in addition to anthrax. The physician's most important responsibility in the control of anthrax is that he should demand that all suspicious lesions be reported to him immediately. Moreover, he should have complete understanding of any government regulations regarding the treatment, disposal, and reporting of communicable disease cases.

The environmental portion of the plant program embraces practically all of the recognized control methods of industrial hygiene as applied to proper plant sanitation. These include the following:

1. Compulsory change of clothing on entering or leaving the plant, together with adequate locker facilities. Preferably there should be two lockers for each employee, one for his street clothes and the other for his work clothes.

2. Protective clothing should be supplied where necessary.

3. Adequate washing facilities, with a supply of towels and hot and cold running water, should be provided. It should be compulsory for all employees exposed to infected material to take a shower before leaving the plant. Time

Three injections of 0.5 ml of antigen at intervals of two weeks were used for immunization of man.

DR. DILKS: I was going to make a statement on cortisone. Cortisone is usually thought to increase the susceptibility to certain viral diseases, and it might preclude its use for anthrax, along with some of the antibiotics.

DR. WILBAR: Is Dr. Mark Allam, the Dean of the School of Veterinary Medicine here at Pennsylvania, still present?

(No response)

I understand that investigators in that school have used penicillin and other antibiotics in the treatment of animals.

DR. CROMARTIE: I wanted to ask Dr. Wedum if he would comment on the serological type of antibody being produced?

DR. WEDUM: This is a matter of authorization to get the information released. I can just say that a great deal of work has been done and the results are encouraging, but I am sorry we can't go into details.

May I ask Dr. Gold a question? In view of his extensive experience, I have been wondering about the extent to which he has observed mixed infections or evidence of mixed infections? I recall that in Ellingson's article there was an instance of a penicillinase producing staphylococcus, which complicated one of the cases and prolonged the period in which the anthrax organism could be isolated from the lesion. Particularly in some of these industrial cases, I should think there might be complicating infection and possibly production of enzymes by organisms which would inactivate either the penicillin or one of the other antibiotics. Any comment?

DR. GOLD: Well, I think invariably you recover -- we have recovered in our cases, a mixed culture. We get anthrax bacilli plus staphylococci or

streptococci in cultures from the lesions and it is quite possible, for example, that the lymphangitis that some of these patients may develop may not actually be the result of the anthrax infection per se, but may be the complicating streptococcus, or hemolytic staphylococcus that they may harbor in the lesion. However, from the time sequence, it is likely that the whole thing is part and parcel of the anthrax infection.

I don't have any bacteriological data and I never ran into the same situation that you mentioned of Ellingson, in which the patient was refractory to penicillin by virtue of the fact that he had an organism of that nature. A great deal depends naturally on the dosage of antibiotic that one uses. We have some patients who required much larger doses, and I don't know whether it was due to the complicating bacterial flora or whether it is due to the organism per se. Different strains of the anthrax bacillus will require much larger doses, because you see the variation in the in vitro tests. Some strains will be inhibited in the range of one-tenth of a unit of penicillin, while others will require as much as one unit, and occasionally some will require as much as five units of penicillin. These were all based on pure anthrax cultures.

DR. WILBAR: Any other questions or comments?

DR. GOLD: I would like to add one comment if I may. With all due respect to our Department of Health I think all the programs that we have outlined are excellent from the point of view of general control, but they have very little effect or influence on anthrax control per se and I think they know it. Because you can have all the toilet facilities you want in the plant, and you can have all the assistance you desire, and by and large you can avoid some contamination, like carrying some infection, but that is only of limited value. I can go into the plant and culture anthrax bacilli from the skin and fingernails of a number of

people and their changing their clothes will not affect the handle of the trolley car that they hold on to when they go home.

I am all for control, that is putting in all kinds of safety measures, etc., but I don't think we ought to delude ourselves that it is specifically aimed at anthrax control because we are not achieving it. The proof is that in the plant that I am concerned with we put all the works in and yet we are getting just as many cases of anthrax as we did before they had a single toilet in the plant. So I think that one must be realistic about it.

I am all for the program, but I don't think we ought to fool ourselves that it is aimed at anthrax control. It will decrease indirectly the incidence if we cut down the number of injuries, but otherwise it will have no effect whatsoever on the incidence of anthrax. The only hope is in the vaccine and the antigen, and I am very anxious to see it put to use, if we can get around the red tape. I, for one, am perfectly willing to start inoculation on a controlled basis as of tomorrow morning if I can get hold of a batch of antigen.

DR. WEDUM: I would like to add a cheerful note to indicate that the Army and Department of Defense and the Chemical Corps have released the antigen as an unclassified item. The method of production is unclassified and is freely available to anyone who wishes to use it.

DR. WILBAR: Dr. Shilen, did you want to comment on the educational features any further?

DR. SHILEN: I think Dr. Gold is correct and I agree with him. We had the industries practice the best of hygiene and we get just as much anthrax in a plant that has a full or part-time physician as in a plant that doesn't have any physician at all.

DR. WILBAR: It is difficult to evaluate the effects of public health ed-

ucation sometimes, but I believe that if the individuals know something about it, it will help in cutting down the incidence.

By the way, the Health Department has tried rather hard, but hasn't been able to find a good anthrax educational movie; we still are looking for one.

If there are no further comments or questions, I know that I can speak for the University of Pennsylvania School of Medicine and the Department of Health of the City of Philadelphia, as well as for the Department of Health of the Commonwealth of Pennsylvania, in saying that we very much appreciate the information the speakers have brought to us today and to all those who entered into the discussion.

You will be interested to know that approximately two hundred people registered today for this session. The proceedings will be published and they will be sent to all who registered and to anyone else who expresses an interest in receiving a copy.

We hope another symposium ten years from now won't be necessary and that the disease will have been better conquered than it has been in the past ten years. We might as well be optimistic about it. Maybe we will have another one ten years from now.

We will consider, then, the symposium adjourned.

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